Figure 1A

1 DIVLTQSPAS LAVSLGQRAT MSCRAGESVD IFGVGFLHWY QQKPGQPPKL

51 LIYRASNLES GIPVRFSGTG SRTDFTLIID PVEADDVATY YCQQTNEDPY

101 TFGGGTKLEI K*GGGGSGGGG SGGGGSGGGG SGGGGSGGGG S*EVQLQQSGA

151 ELVEPGASVK LSCTASGFNI KDTYMHWVKQ RPEQGLEWIG RIDPANGNSK

201 YVPKFQGKAT ITADTSSNTA YLQLTSLTSE DTAVYYCAPF GYYVSDYAMA

251 YWGQGTSVTV SS

Figure 1B

```
  1    GACATCGTCC TGACCCAGAG CCCGGCAAGC CTGGCTGTTT CCCTGGGCCA
 51    GCGTGCCACT ATGTCCTGCA GAGCGGGTGA GTCTGTTGAC ATTTTCGGTG
101    TCGGTTTTCT GCACTGGTAC CAACAGAAAC CGGGTCAGCC GCCAAAACTG
151    CTGATCTATC GTGCTTCTAA CCTGGAGTCC GGCATCCCGG TACGTTTCTC
201    CGGTACTGGC TCTCGTACTG ATTTTACCCT GATTATCGAC CCGGTGGAAG
251    CAGACGATGT TGCCACCTAC TATTGCCAGC AGACCAACGA GGATCCGTAC
301    ACCTTCGGTG GCGGTACTAA ACTGGAGATC AAAGGCGGTG GTGGTTCTGG
351    TGGTGGTGGT AGCGGCGGCG GTGGTAGCGG TGGCGGTGGC AGCGGTGGTG
401    GTGGCTCTGG TGGCGGTGGC TCTGAAGTGC AGCTGCAGCA GTCCGGTGCG
451    GAGCTCGTTG AACCGGGCGC TTCTGTGAAA CTGTCTTGCA CTGCATCTGG
501    TTTCAACATT AAGGACACCT ACATGCACTG GGTGAAACAA CGCCCGGAAC
551    AGGGTCTGGA GTGGATCGGT CGCATCGATC CGGCTAACGG TAACAGCAAA
601    TACGTGCCAA AATTCCAGGG TAAAGCAACC ATCACTGCTG ATACCTCCTC
651    TAACACTGCT TACCTGCAGC TGACTTCCCT GACTAGCGAA GACACCGCGG
701    TTTATTACTG CGCTCCGTTC GGCTACTATG TCAGCGATTA CGCAATGGCC
751    TACTGGGGTC AGGGCACCTC TGTTACCGTT TCTAGC
```

Figure 1C

263 TPVSEKQL AEVVANTITP LMKAQSVPGM AVAVIYQGKP

301 HYYTFGKADI AANKPVTPQT LFELGSISKT FTGVLGGDAI ARGEISLDDA

351 VTRYWPQLTG KQWQGIRMLD LATYTAGGLP LQVPDEVTDN ASLLRFYQNW

401 QPQWKPGTTR LYANASIGLF GALAVKPSGM PYEQAMTTRV LKPLKLDHTW

451 INVPKAEEAH YAWGYRDGKA VRVSPGMLDA QAYGVKTNVQ DMANWVMANM

501 APENVADASL KQGIALAQSR YWRIGSMYQG LGWEMLNWPV EANTVVETSF

551 GNVALAPLPV AEVNPPAPPV KASWVHKTGS TGGFGSYVAF IPEKQIGIVM

602 LANTSYPNPA RVEAAYHILE ALQ

Figure 1D

```
   1  ACACCGGTGT CAGAAAAACA GCTGGCGGAG GTGGTCGCGA ATACGATTAC
  51  CCCGCTGATG AAAGCCCAGT CTGTTCCAGG CATGGCGGTG GCCGTTATTT
 101  ATCAGGGAAA ACCGCACTAT TACACATTTG GCAAGGCCGA TATCGCGGCG
 151  AATAAACCCG TTACGCCTCA GACCCTGTTC GAGCTGGGTT CTATAAGTAA
 201  AACCTTCACC GGCGTTTTAG GTGGGGATGC CATTGCTCGC GGTGAAATTT
 251  CGCTGGACGA TGCGGTGACC AGATACTGGC CACAGCTGAC GGGCAAGCAG
 301  TGGCAGGGTA TTCGTATGCT GGATCTCGCC ACCTACACCG CTGGCGGCCT
 351  GCCGCTACAG GTACCGGATG AGGTCACGGA TAACGCCTCC CTGCTGCGCT
 401  TTTATCAAAA CTGGCAGCCG CAGTGGAAGC CTGGCACAAC GCGTCTTTAC
 451  GCCAACGCCA GCATCGGTCT TTTTGGTGCG CTGGCGGTCA AACCTTCTGG
 501  CATGCCCTAT GAGCAGGCCA TGACGACGCG GGTCCTTAAG CCGCTCAAGC
 551  TGGACCATAC CTGGATTAAC GTGCCGAAAG CGGAAGAGGC GCATTACGCC
 601  TGGGGCTATC GTGACGGTAA AGCGGTGCGC GTTTCGCCGG GTATGCTGGA
 651  TGCACAAGCC TATGGCGTGA AAACCAACGT GCAGGATATG GCGAACTGGG
 701  TCATGGCAAA CATGGCGCCG GAGAACGTTG CTGATGCCTC ACTTAAGCAG
 751  GGCATCGCGC TGGCGCAGTC GCGCTACTGG CGTATCGGGT CAATGTATCA
 801  GGGTCTGGGC TGGGAGATGC TCAACTGGCC CGTGGAGGCC AACACGGTGG
 851  TCGAGACGAG TTTTGGTAAT GTAGCACTGG CGCCGTTGCC CGTGGCAGAA
 901  GTGAATCCAC CGGCTCCCCC GGTCAAAGCG TCCTGGGTCC ATAAAACGGG
 951  CTCTACTGGC GGGTTTGGCA GCTACGTGGC CTTTATTCCT GAAAAGCAGA
1001  TCGGTATTGT GATGCTCGCG AATACAAGCT ATCCGAACCC GGCACGCGTT
1051  GAGGCGGCAT ACCATATCCT CGAGGCGCTA CAG
```

Figure 1E

1 DIVLTQSPAS LAVSLGQRAT MSCRAGESVD IFGVGFLHWY QQKPGQPPKL

51 LIYRASNLES GIPVRFSGTG SRTDFTLIID PVEADDVATY YCQQTNEDPY

101 TFGGGTKLEI K*GGGGSGGGG SGGGGSGGGG SGGGGSGGGG S*EVQLQQSGA

151 ELVEPGASVK LSCTASGFNI KDTYMHWVKQ RPEQGLEWIG RIDPANGNSK

201 YVPKFQGKAT ITADTSSNTA YLQLTSLTSE DTAVYYCAPF GYYVSDYAMA

251 YWGQGTSVTV SSTPVSEKQL AEVVANTITP LMKAQSVPGM AVAVIYQGKP

301 HYYTFGKADI AANKPVTPQT LFELGSISKT FTGVLGGDAI ARGEISLDDA

351 VTRYWPQLTG KQWQGIRMLD LATYTAGGLP LQVPDEVTDN ASLLRFYQNW

401 QPQWKPGTTR LYANASIGLF GALAVKPSGM PYEQAMTTRV LKPLKLDHTW

451 INVPKAEEAH YAWGYRDGKA VRVSPGMLDA QAYGVKTNVQ DMANWVMANM

501 APENVADASL KQGIALAQSR YWRIGSMYQG LGWEMLNWPV EANTVVETSF

551 GNVALAPLPV AEVNPPAPPV KASWVHKTGS TGGFGSYVAF IPEKQIGIVM

601 LANTSYPNPA RVEAAYHILE ALQ

Figure 1F

```
   1  GACATCGTCC TGACCCAGAG CCCGGCAAGC CTGGCTGTTT
  CCCTGGGCCA
  51  GCGTGCCACT ATGTCCTGCA GAGCGGGTGA GTCTGTTGAC
  ATTTTCGGTG
 101  TCGGTTTTCT GCACTGGTAC CAACAGAAAC CGGGTCAGCC
  GCCAAAACTG
 151  CTGATCTATC GTGCTTCTAA CCTGGAGTCC GGCATCCCGG
  TACGTTTCTC
 201  CGGTACTGGC TCTCGTACTG ATTTTACCCT GATTATCGAC
  CCGGTGGAAG
 251  CAGACGATGT TGCCACCTAC TATTGCCAGC AGACCAACGA
  GGATCCGTAC
 301  ACCTTCGGTG GCGGTACTAA ACTGGAGATC AAAGGCGGTG
  GTGGTTCTGG
 351  TGGTGGTGGT AGCGGCGGCG GTGGTAGCGG TGGCGGTGGC
  AGCGGTGGTG
 401  GTGGCTCTGG TGGCGGTGGC TCTGAAGTGC AGCTGCAGCA
  GTCCGGTGCG
 451  GAGCTCGTTG AACCGGGCGC TTCTGTGAAA CTGTCTTGCA
  CTGCATCTGG
 501  TTTCAACATT AAGGACACCT ACATGCACTG GGTGAAACAA
  CGCCCGGAAC
 551  AGGGTCTGGA GTGGATCGGT CGCATCGATC CGGCTAACGG
  TAACAGCAAA
 601  TACGTGCCAA AATTCCAGGG TAAAGCAACC ATCACTGCTG
  ATACCTCCTC
 651  TAACACTGCT TACCTGCAGC TGACTTCCCT GACTAGCGAA
  GACACCGCGG
 701  TTTATTACTG CGCTCCGTTC GGCTACTATG TCAGCGATTA
  CGCAATGGCC
 751  TACTGGGGTC AGGGCACCTC TGTTACCGTT TCTAGCACAC
  CGGTGTCAGA
 801  AAAACAGCTG GCGGAGGTGG TCGCGAATAC GATTACCCCG
  CTGATGAAAG
 851  CCCAGTCTGT TCCAGGCATG GCGGTGGCCG TTATTTATCA
  GGGAAAACCG
 901  CACTATTACA CATTTGGCAA GGCCGATATC GCGGCGAATA
  AACCCGTTAC
 951  GCCTCAGACC CTGTTCGAGC TGGGTTCTAT AAGTAAAACC
  TTCACCGGCG
1001  TTTTAGGTGG GGATGCCATT GCTCGCGGTG AAATTTCGCT
  GGACGATGCG
1051  GTGACCAGAT ACTGGCCACA GCTGACGGGC AAGCAGTGGC
  AGGGTATTCG
```

1101 TATGCTGGAT CTCGCCACCT ACACCGCTGG CGGCCTGCCG
CTACAGGTAC
1151 CGGATGAGGT CACGGATAAC GCCTCCCTGC TGCGCTTTTA
TCAAAACTGG
1201 CAGCCGCAGT GGAAGCCTGG CACAACGCGT CTTTACGCCA
ACGCCAGCAT
1251 CGGTCTTTTT GGTGCGCTGG CGGTCAAACC TTCTGGCATG
CCCTATGAGC
1301 AGGCCATGAC GACGCGGGTC CTTAAGCCGC TCAAGCTGGA
CCATACCTGG
1351 ATTAACGTGC CGAAAGCGGA AGAGGCGCAT TACGCCTGGG
GCTATCGTGA
1401 CGGTAAAGCG GTGCGCGTTT CGCCGGGTAT GCTGGATGCA
CAAGCCTATG
1451 GCGTGAAAAC CAACGTGCAG GATATGGCGA ACTGGGTCAT
GGCAAACATG
1501 GCGCCGGAGA ACGTTGCTGA TGCCTCACTT AAGCAGGGCA
TCGCGCTGGC
1551 GCAGTCGCGC TACTGGCGTA TCGGGTCAAT GTATCAGGGT
CTGGGCTGGG
1601 AGATGCTCAA CTGGCCCGTG GAGGCCAACA CGGTGGTCGA
GACGAGTTTT
1651 GGTAATGTAG CACTGGCGCC GTTGCCCGTG GCAGAAGTGA
ATCCACCGGC
1701 TCCCCCGGTC AAAGCGTCCT GGGTCCATAA AACGGGCTCT
ACTGGCGGGT
1751 TTGGCAGCTA CGTGGCCTTT ATTCCTGAAA AGCAGATCGG
TATTGTGATG
1801 CTCGCGAATA CAAGCTATCC GAACCCGGCA CGCGTTGAGG
CGGCATACCA
1851 TATCCTCGAG GCGCTACAG

Figure 2A

DIVLTQSPAS LSVSLGQRAT MSCRAGESVD IFGVGFLHWY QQKPGQPPKL

51 LIYRASNLES GIPVRFSGTG SGTDFTLIID PVEADDVATY YCQQTNEDPY

101 TFGGGTKLEI K*GGGGSGGGG SGGGGSGGGG SGGGGSGGGG S*EVQLQQSGA

151 ELVEPGASVK LSCTASGFNI KDTYMHWVKQ RPEQGLEWIG RIDPANGNSK

201 YVPKFQGKAT ITADTSSNTA YLQLTSLTSE DTAVYYCAPF GYYVSDYAMA

251 YWGQGTSVTV SS

Figure 2B

```
  1   GACATCGTCC TGACCCAGAG CCCGGCAAGC CTGTCTGTTT CCCTGGGCCA
 51   GCGTGCCACT ATGTCCTGCA GAGCGGGTGA GTCTGTTGAC ATTTTCGGTG
101   TCGGTTTTCT GCACTGGTAC CAACAGAAAC CGGGTCAGCC GCCAAAACTG
151   CTGATCTATC GTGCTTCTAA CCTGGAGTCC GGCATCCCGG TACGTTTCTC
201   CGGTACTGGC TCTGGTACTG ATTTTACCCT GATTATCGAC CCGGTGGAAG
251   CAGACGATGT TGCCACCTAC TATTGCCAGC AGACCAACGA GGATCCGTAC
301   ACCTTCGGTG GCGGTACTAA ACTGGAGATC AAAGGCGGTG GTGGTTCTGG
351   TGGTGGTGGT AGCGGTGGCG GTGGTAGCGG TGGCGGTGGC AGCGGTGGTG
401   GTGGCTCTGG TGGCGGTGGC TCTGAAGTGC AGCTGCAGCA GTCCGGTGCG
451   GAGCTCGTTG AACCGGGCGC TTCTGTGAAA CTGTCTTGCA CTGCATCTGG
501   TTTCAACATT AAGGACACCT ACATGCACTG GGTGAAACAA CGCCCGGAAC
551   AGGGTCTGGA GTGGATCGGT CGCATCGATC CGGCTAACGG TAACAGCAAA
601   TACGTGCCAA AATTCCAGGG TAAAGCAACC ATCACTGCTG ATACCTCCTC
651   TAACACTGCT TACCTGCAGC TGACTTCCCT GACTAGCGAA GACACCGCGG
701   TTTATTACTG CGCTCCGTTC GGCTACTATG TCAGCGATTA CGCAATGGCC
751   TACTGGGGTC AGGGCACCTC TGTTACCGTT TCTAGC
```

Figure 3

262 TPVSEKQL AEVVANTITP LMAAQSVPGM AVAVIYQGKP

301 HYYTFGKADI AANKPVTPQT LFELGSISKT FTGVLGGDAI ARGEISLDDA

351 VTRYWPQLTG KQWQGIRMLD LATYTAGGLP LQVPDEVTDN ASLLRFYQNW

401 QPQWKPGTTR LYANASIGLF GALAVKPSGM PYEQAMTTRV LKPLKLDHTW

451 INVPKAEEAH YAWGYRDGKA VRVSPGMLDA QAYGVKTNVQ DMANWVMANM

501 APENVADASL KQGIALAQSR YWRIGSMYQG LGWEMLNWPV EANTVVETSF

551 GNVALAPLPV AEVNPPAPPV KASWVHKTGS TGGFGAYVAF IPEKQIGIVM

601 LANTSYPNPA RVEAAYHILE ALQ

Figure 4A

1 DIVLTQSPAS LSVSLGQRAT MSCRAGESVD IFGVGFLHWY QQKPGQPPKL

51 LIYRASNLES GIPVRFSGTG SGTDFTLIID PVEADDVATY YCQQTNEDPY

101 TFGGGTKLEI K*GGGGSGGGG SGGGGSGGGG SGGGGSGGGG S*EVQLQQSGA

151 ELVEPGASVK LSCTASGFNI KDTYMHWVKQ RPEQGLEWIG RIDPANGNSK

201 YVPKFQGKAT ITADTSSNTA YLQLTSLTSE DTAVYYCAPF GYYVSDYAMA

251 YWGQGTSVTV SSTPVSEKQL AEVVANTITP LMKAQSVPGM AVAVIYQGKP

301 HYYTFGKADI AANKPVTPQT LFELGSISKT FTGVLGGDAI ARGEISLDDA

351 VTRYWPQLTG KQWQGIRMLD LATYTAGGLP LQVPDEVTDN ASLLRFYQNW

401 QPQWKPGTTR LYANASIGLF GALAVKPSGM PYEQAMTTRV LKPLKLDHTW

451 INVPKAEEAH YAWGYRDGKA VRVSPGMLDA QAYGVKTNVQ DMANWVMANM

501 APENVADASL KQGIALAQSR YWRIGSMYQG LGWEMLNWPV EANTVVETSF

551 GNVALAPLPV AEVNPPAPPV KASWVHKTGS TGGFGSYVAF IPEKQIGIVM

601 LANTSYPNPA RVEAAYHILE ALQ

Figure 4B

```
   1.  GACATCGTCC TGACCCAGAG CCCGGCAAGC CTGTCTGTTT CCCTGGGCCA
  51   GCGTGCCACT ATGTCCTGCA GAGCGGGTGA GTCTGTTGAC ATTTTCGGTG
 101   TCGGTTTTCT GCACTGGTAC CAACAGAAAC CGGGTCAGCC GCCAAAACTG
 151   CTGATCTATC GTGCTTCTAA CCTGGAGTCC GGCATCCCGG TACGTTTCTC
 201   CGGTACTGGC TCTGGTACTG ATTTTACCCT GATTATCGAC CCGGTGGAAG
 251   CAGACGATGT TGCCACCTAC TATTGCCAGC AGACCAACGA GGATCCGTAC
 301   ACCTTCGGTG GCGGTACTAA ACTGGAGATC AAAGGCGGTG GTGGTTCTGG
 351   TGGTGGTGGT AGCGGTGGCG GTGGTAGCGG TGGCGGTGGC AGCGGTGGTG
 401   GTGGCTCTGG TGGCGGTGGC TCTGAAGTGC AGCTGCAGCA GTCCGGTGCG
 451   GAGCTCGTTG AACCGGGCGC TTCTGTGAAA CTGTCTTGCA CTGCATCTGG
 501   TTTCAACATT AAGGACACCT ACATGCACTG GGTGAAACAA CGCCCGGAAC
 551   AGGGTCTGGA GTGGATCGGT CGCATCGATC CGGCTAACGG TAACAGCAAA
 601   TACGTGCCAA AATTCCAGGG TAAAGCAACC ATCACTGCTG ATACCTCCTC
 651   TAACACTGCT TACCTGCAGC TGACTTCCCT GACTAGCGAA GACACCGCGG
 701   TTTATTACTG CGCTCCGTTC GGCTACTATG TCAGCGATTA CGCAATGGCC
 751   TACTGGGGTC AGGGCACCTC TGTTACCGTT TCTAGCACAC CGGTGTCAGA
 801   AAAACAGCTG GCGGAGGTGG TCGCGAATAC GATTACCCCG CTGATGAAAG
 851   CCCAGTCTGT TCCAGGCATG GCGGTGGCCG TTATTTATCA GGGAAAACCG
 901   CACTATTACA CATTTGGCAA GGCCGATATC GCGGCGAATA AACCCGTTAC
 951   GCCTCAGACC CTGTTCGAGC TGGGTTCTAT AAGTAAAACC TTCACCGGCG
1001   TTTTAGGTGG GGATGCCATT GCTCGCGGTG AAATTTCGCT GGACGATGCG
1051   GTGACCAGAT ACTGGCCACA GCTGACGGGC AAGCAGTGGC AGGGTATTCG
1101   TATGCTGGAT CTCGCCACCT ACACCGCTGG CGGCCTGCCG CTACAGGTAC
1151   CGGATGAGGT CACGGATAAC GCCTCCCTGC TGCGCTTTTA TCAAAACTGG
1201   CAGCCGCAGT GGAAGCCTGG CACAACGCGT CTTTACGCCA ACGCCAGCAT
1251   CGGTCTTTTT GGTGCGCTGG CGGTCAAACC TTCTGGCATG CCCTATGAGC
1301   AGGCCATGAC GACGCGGGTC CTTAAGCCGC TCAAGCTGGA CCATACCTGG
1351   ATTAACGTGC CGAAAGCGGA AGAGGCGCAT TACGCCTGGG GCTATCGTGA
1401   CGGTAAAGCG GTGCGCGTTT CGCCGGGTAT GCTGGATGCA CAAGCCTATG
1451   GCGTGAAAAC CAACGTGCAG GATATGGCGA ACTGGGTCAT GGCAAACATG
1501   GCGCCGGAGA ACGTTGCTGA TGCCTCACTT AAGCAGGGCA TCGCGCTGGC
1551   GCAGTCGCGC TACTGGCGTA TCGGGTCAAT GTATCAGGGT CTGGGCTGGG
1601   AGATGCTCAA CTGGCCCGTG GAGGCCAACA CGGTGGTCGA GACGAGTTTT
1651   GGTAATGTAG CACTGGCGCC GTTGCCCGTG GCAGAAGTGA ATCCACCGGC
1701   TCCCCCGGTC AAAGCGTCCT GGGTCCATAA AACGGGCTCT ACTGGCGGGT
1751   TTGGCAGCTA CGTGGCCTTT ATTCCTGAAA AGCAGATCGG TATTGTGATG
1801   CTCGCGAATA CAAGCTATCC GAACCCGGCA CGCGTTGAGG CGGCATACCA
1851   TATCCTCGAG GCGCTACAG
```

Figure 4C

1 DIVLTQSPAS L**S**VSLGQRAT MSCRAGESVD IFGVGFLHWY QQKPGQPPKL

51 LIYRASNLES GIPVRFSGTG S**G**TDFTLIID PVEADDVATY YCQQTNEDPY

101 TFGGGTKLEI K*GGGGSGGGG SGGGGSGGGG SGGGGSGGGG S*EVQLQQSGA

151 ELVEPGASVK LSCTASGFNI KDTYMHWVKQ RPEQGLEWIG RIDPANGNSK

201 YVPKFQGKAT ITADTSSNTA YLQLTSLTSE DTAVYYCAPF GYYVSDYAMA

251 YWGQGTSVTV SSTPVSEKQL AEVVANTITP LM**A**AQSVPGM AVAVIYQGKP

301 HYYTFGKADI AANKPVTPQT LFELGSISKT FTGVLGGDAI ARGEISLDDA

351 VTRYWPQLTG KQWQGIRMLD LATYTAGGLP LQVPDEVTDN ASLLRFYQNW

401 QPQWKPGTTR LYANASIGLF GALAVKPSGM PYEQAMTTRV LKPLKLDHTW

451 INVPKAEEAH YAWGYRDGKA VRVSPGMLDA QAYGVKTNVQ DMANWVMANM

501 APENVADASL KQGIALAQSR YWRIGSMYQG LGWEMLNWPV EANTVVETSF

551 GNVALAPLPV AEVNPPAPPV KASWVHKTGS TGGFG**A**YVAF IPEKQIGIVM

601 LANTSYPNPA RVEAAYHILE ALQ

Figure 4D

```
   1  GACATCGTCC TGACCCAGAG CCCGGCAAGC CTGTCTGTTT CCCTGGGCCA
  51  GCGTGCCACT ATGTCCTGCA GAGCGGGTGA GTCTGTTGAC ATTTTCGGTG
 101  TCGGTTTTCT GCACTGGTAC CAACAGAAAC CGGGTCAGCC GCCAAAACTG
 151  CTGATCTATC GTGCTTCTAA CCTGGAGTCC GGCATCCCGG TACGTTTCTC
 201  CGGTACTGGC TCTGGTACTG ATTTTACCCT GATTATCGAC CCGGTGGAAG
 251  CAGACGATGT TGCCACCTAC TATTGCCAGC AGACCAACGA GGATCCGTAC
 301  ACCTTCGGTG GCGGTACTAA ACTGGAGATC AAAGGCGGTG GTGGTTCTGG
 351  TGGTGGTGGT AGCGGTGGCG GTGGTAGCGG TGGCGGTGGC AGCGGTGGTG
 401  GTGGCTCTGG TGGCGGTGGC TCTGAAGTGC AGCTGCAGCA GTCCGGTGCG
 451  GAGCTCGTTG AACCGGGCGC TTCTGTGAAA CTGTCTTGCA CTGCATCTGG
 501  TTTCAACATT AAGGACACCT ACATGCACTG GGTGAAACAA CGCCCGGAAC
 551  AGGGTCTGGA GTGGATCGGT CGCATCGATC CGGCTAACGG TAACAGCAAA
 601  TACGTGCCAA AATTCCAGGG TAAAGCAACC ATCACTGCTG ATACCTCCTC
 651  TAACACTGCT TACCTGCAGC TGACTTCCCT GACTAGCGAA GACACCGCGG
 701  TTTATTACTG CGCTCCGTTC GGCTACTATG TCAGCGATTA CGCAATGGCC
 751  TACTGGGGTC AGGGCACCTC TGTTACCGTT TCTAGCACAC CGGTGTCAGA
 801  AAAACAGCTG GCGGAGGTGG TCGCGAATAC GATTACCCCG CTGATGGCGG
 851  CCCAGTCTGT TCCAGGCATG GCGGTGGCCG TTATTTATCA GGGAAAACCG
 901  CACTATTACA CATTTGGCAA GGCCGATATC GCGGCGAATA AACCCGTTAC
 951  GCCTCAGACC CTGTTCGAGC TGGGTTCTAT AAGTAAAACC TTCACCGGCG
1001  TTTTAGGTGG GGATGCCATT GCTCGCGGTG AAATTTCGCT GGACGATGCG
1051  GTGACCAGAT ACTGGCCACA GCTGACGGGC AAGCAGTGGC AGGGTATTCG
1101  TATGCTGGAT CTCGCCACCT ACACCGCTGG CGGCCTGCCG CTACAGGTAC
1151  CGGATGAGGT CACGGATAAC GCCTCCCTGC TGCGCTTTTA TCAAAACTGG
1201  CAGCCGCAGT GGAAGCCTGG CACAACGCGT CTTTACGCCA ACGCCAGCAT
1251  CGGTCTTTTT GGTGCGCTGG CGGTCAAACC TTCTGGCATG CCCTATGAGC
1301  AGGCCATGAC GACGCGGGTC CTTAAGCCGC TCAAGCTGGA CCATACCTGG
1351  ATTAACGTGC CGAAAGCGGA AGAGGCGCAT TACGCCTGGG GCTATCGTGA
1401  CGGTAAAGCG GTGCGCGTTT CGCCGGGTAT GCTGGATGCA CAAGCCTATG
1451  GCGTGAAAAC CAACGTGCAG GATATGGCGA ACTGGGTCAT GGCAAACATG
1501  GCGCCGGAGA ACGTTGCTGA TGCCTCACTT AAGCAGGGCA TCGCGCTGGC
1551  GCAGTCGCGC TACTGGCGTA TCGGGTCAAT GTATCAGGGT CTGGGCTGGG
1601  AGATGCTCAA CTGGCCCGTG GAGGCCAACA CGGTGGTCGA GACGAGTTTT
1651  GGTAATGTAG CACTGGCGCC GTTGCCCGTG GCAGAAGTGA ATCCACCGGC
1701  TCCCCCGGTC AAAGCGTCCT GGGTCCATAA AACGGGCTCT ACTGGCGGGT
1751  TTGGCGCGTA CGTGGCCTTT ATTCCTGAAA AGCAGATCGG TATTGTGATG
1801  CTCGCGAATA CAAGCTATCC GAACCCGGCA CGCGTTGAGG CGGCATACCA
1851  TATCCTCGAG GCGCTACAG
```

Figure 4E

```
   1  AGGAATTATC ATATGAAATA CCTGCTGCCG ACCGCTGCTG
  CTGGTCTGCT
  51  GCTCCTCGCT GCCCAGCCGG CCATGGCCGA CATCGTCCTG
  ACCCAGAGCC
 101  CGGCAAGCCT GTCTGTTTCC CTGGGCCAGC GTGCCACTAT
  GTCCTGCAGA
 151  GCGGGTGAGT CTGTTGACAT TTTCGGTGTC GGTTTTCTGC
  ACTGGTACCA
 201  ACAGAAACCG GGTCAGCCGC CAAAACTGCT GATCTATCGT
  GCTTCTAACC
 251  TGGAGTCCGG CATCCCGGTA CGTTTCTCCG GTACTGGCTC
  TGGTACTGAT
 301  TTTACCCTGA TTATCGACCC GGTGGAAGCA GACGATGTTG
  CCACCTACTA
 351  TTGCCAGCAG ACCAACGAGG ATCCGTACAC CTTCGGTGGC
  GGTACTAAAC
 401  TGGAGATCAA AGGCGGTGGT GGTTCTGGTG GTGGTGGTAG
  CGGTGGCGGT
 451  GGTAGCGGTG GCGGTGGCAG CGGTGGTGGT GGCTCTGGTG
  GCGGTGGCTC
 501  TGAAGTGCAG CTGCAGCAGT CCGGTGCGGA GCTCGTTGAA
  CCGGGCGCTT
 551  CTGTGAAACT GTCTTGCACT GCATCTGGTT TCAACATTAA
  GGACACCTAC
 601  ATGCACTGGG TGAAACAACG CCCGGAACAG GGTCTGGAGT
  GGATCGGTCG
 651  CATCGATCCG GCTAACGGTA ACAGCAAATA CGTGCCAAAA
  TTCCAGGGTA
 701  AAGCAACCAT CACTGCTGAT ACCTCCTCTA ACACTGCTTA
  CCTGCAGCTG
 751  ACTTCCCTGA CTAGCGAAGA CACCGCGGTT TATTACTGCG
  CTCCGTTCGG
 801  CTACTATGTC AGCGATTACG CAATGGCCTA CTGGGGTCAG
  GGCACCTCTG
 851  TTACCGTTTC TAGCACACCG GTGTCAGAAA AACAGCTGGC
  GGAGGTGGTC
 901  GCGAATACGA TTACCCCGCT GATGGCGGCC CAGTCTGTTC
  CAGGCATGGC
 951  GGTGGCCGTT ATTTATCAGG GAAAACCGCA CTATTACACA
  TTTGGCAAGG
1001  CCGATATCGC GGCGAATAAA CCCGTTACGC CTCAGACCCT
  GTTCGAGCTG
```

1051 GGTTCTATAA GTAAAACCTT CACCGGCGTT TTAGGTGGGG
ATGCCATTGC
1101 TCGCGGTGAA ATTTCGCTGG ACGATGCGGT GACCAGATAC
TGGCCACAGC
1151 TGACGGGCAA GCAGTGGCAG GGTATTCGTA TGCTGGATCT
CGCCACCTAC
1201 ACCGCTGGCG GCCTGCCGCT ACAGGTACCG GATGAGGTCA
CGGATAACGC
1251 CTCCCTGCTG CGCTTTTATC AAAACTGGCA GCCGCAGTGG
AAGCCTGGCA
1301 CAACGCGTCT TTACGCCAAC GCCAGCATCG GTCTTTTTGG
TGCGCTGGCG
1351 GTCAAACCTT CTGGCATGCC CTATGAGCAG GCCATGACGA
CGCGGGTCCT
1401 TAAGCCGCTC AAGCTGGACC ATACCTGGAT TAACGTGCCG
AAAGCGGAAG
1451 AGGCGCATTA CGCCTGGGGC TATCGTGACG GTAAAGCGGT
GCGCGTTTCG
1501 CCGGGTATGC TGGATGCACA AGCCTATGGC GTGAAAACCA
ACGTGCAGGA
1551 TATGGCGAAC TGGGTCATGG CAAACATGGC GCCGGAGAAC
GTTGCTGATG
1601 CCTCACTTAA GCAGGGCATC GCGCTGGCGC AGTCGCGCTA
CTGGCGTATC
1651 GGGTCAATGT ATCAGGGTCT GGGCTGGGAG ATGCTCAACT
GGCCCGTGGA
1701 GGCCAACACG GTGGTCGAGA CGAGTTTTGG TAATGTAGCA
CTGGCGCCGT
1751 TGCCCGTGGC AGAAGTGAAT CCACCGGCTC CCCCGGTCAA
AGCGTCCTGG
1801 GTCCATAAAA CGGGCTCTAC TGGCGGGTTT GGCGCGTACG
TGGCCTTTAT
1851 TCCTGAAAAG CAGATCGGTA TTGTGATGCT CGCGAATACA
AGCTATCCGA
1901 ACCCGGCACG CGTTGAGGCG GCATACCATA TCCTCGAGGC
GCTACAGTAG
1951 GAATTCGAGC TCCGTCGACA AGCTTGCGGC CGCACTCGAG
ATCAAACGGG
2001 CTAGCCAGCC AGAACTCGCC CCGGAAGACC CCGAGGATGT
CGAGCACCAC
2051 CACCACCACC ACTGAGATCC GGCTGCTAAC AAAGCCCGAA
AGGAAGCTGA
2101 GTTGGCTGCT GCCACCGCTG AGCAATAACT AGCATAACCC
CTTGGGGCCT
2151 CTAAACGGGT CTTGAGGGGT TTTTTGCTGA AAGGAGGAAC
TATATCCGGA

2201 TTGGCGAATG GGACGCGCCC TGTAGCGGCG CATTAAGCGC
GGCGGGTGTG
2251 GTGGTTACGC GCAGCGTGAC CGCTACACTT GCCAGCGCCC
TAGCGCCCGC
2301 TCCTTTCGCT TTCTTCCCTT CCTTTCTCGC CACGTTCGCC
GGCTTTCCCC
2351 GTCAAGCTCT AAATCGGGGG CTCCCTTTAG GGTTCCGATT
TAGTGCTTTA
2401 CGGCACCTCG ACCCCAAAAA ACTTGATTAG GGTGATGGTT
CACGTAGTGG
2451 GCCATCGCCC TGATAGACGG TTTTTCGCCC TTTGACGTTG
GAGTCCACGT
2501 TCTTTAATAG TGGACTCTTG TTCCAAACTG GAACAACACT
CAACCCTATC
2551 TCGGTCTATT CTTTTGATTT ATAAGGGATT TTGCCGATTT
CGGCCTATTG
2601 GTTAAAAAAT GAGCTGATTT AACAAAAATT TAACGCGAAT
TTTAACAAAA
2651 TATTAACGCT TACAATTTCC TGATGCGGTA TTTTCTCCTT
ACGCATCTGT
2701 GCGGTATTTC ACACCGCATA TGGTGCACTC TCAGTACAAT
CTGCTCTGAT
2751 GCCGCATAGT TAAGCCAGCC CCGACACCCG CCAACACCCG
CTGACGCGCC
2801 CTGACGGGCT TGTCTGCTCC CGGCATCCGC TTACAGACAA
GCTGTGACCG
2851 TCTCCGGGAG CTGCATGTGT CAGAGGTTTT CACCGTCATC
ACCGAAACGC
2901 GCGAGACGAA AGGGCCTCGT GATACGCCTA TTTTTATAGG
TTAATGTCAT
2951 GATAATAATG GTTTCTTAGA CGTCAGGTGG CACTTTTCGG
GGAAATGTGC
3001 GCGGAACCCC TATTTGTTTA TTTTTCTAAA TACATTCAAA
TATGTATCCG
3051 CTCATGAGAC AATAACCCTG TGGCAGCATC ACCCGACGCA
CTTTGCGCCG
3101 AATAAATACC TGTGACGGAA GATCACTTCG CAGAATAAAT
AAATCCTGGT
3151 GTCCCTGTTG ATACCGGGAA GCCCTGGGCC AACTTTTGGC
GAAAATGAGA
3201 CGTTGATCGG CACGTAAGAG GTTCCAACTT TCACCATAAT
GAAATAAGAT
3251 CACTACCGGG CGTATTTTTT GAGTTATCGA GATTTTCAGG
AGCTAAGGAA
3301 GCTAAAATGG AGAAAAAAAT CACTGGATAT ACCACCGTTG
ATATATCCCA

3351 ATGGCATCGT AAAGAACATT TTGAGGCATT TCAGTCAGTT
GCTCAATGTA
3401 CCTATAACCA GACCGTTCAG CTGGATATTA CGGCCTTTTT
AAAGACCGTA
3451 AAGAAAAATA AGCACAAGTT TTATCCGGCC TTTATTCACA
TTCTTGCCCG
3501 CCTGATGAAT GCTCATCCGG AATTCCGTAT GGCAATGAAA
GACGGTGAGC
3551 TGGTGATATG GGATAGTGTT CACCCTTGTT ACACCGTTTT
CCATGAGCAA
3601 ACTGAAACGT TTTCATCGCT CTGGAGTGAA TACCACGACG
ATTTCCGGCA
3651 GTTTCTACAC ATATATTCGC AAGATGTGGC GTGTTACGGT
GAAAACCTGG
3701 CCTATTTCCC TAAAGGGTTT ATTGAGAATA TGTTTTTCGT
CTCAGCCAAT
3751 CCCTGGGTGA GTTTCACCAG TTTTGATTTA AACGTGGCCA
ATATGGACAA
3801 CTTCTTCGCC CCCGTTTTCA CGATGGGCAA ATATTATACG
CAAGGCGACA
3851 AGGTGCTGAT GCCGCTGGCG ATTCAGGTTC ATCATGCCGT
CTGTGATGGC
3901 TTCCATGTCG GCAGAATGCT TAATGAATTA CAACAGTACT
GCGATGAGTG
3951 GCAGGGCGGG GCGTAAAGAC AGATCGCTGA GATAGGTGCC
TCACTGATTA
4001 AGCATTGGTA ACTGTCAGAC CAAGTTTACT CATATATACT
TTAGATTGAT
4051 TTAAAACTTC ATTTTTAATT TAAAAGGATC TAGGTGAAGA
TCCTTTTTGA
4101 TAATCTCATG ACCAAAATCC CTTAACGTGA GTTTTCGTTC
CACTGAGCGT
4151 CAGACCCCGT AGAAAAGATC AAAGGATCTT CTTGAGATCC
TTTTTTTCTG
4201 CGCGTAATCT GCTGCTTGCA AACAAAAAAA CCACCGCTAC
CAGCGGTGGT
4251 TTGTTTGCCG GATCAAGAGC TACCAACTCT TTTTCCGAAG
GTAACTGGCT
4301 TCAGCAGAGC GCAGATACCA AATACTGTTC TTCTAGTGTA
GCCGTAGTTA
4351 GGCCACCACT TCAAGAACTC TGTAGCACCG CCTACATACC
TCGCTCTGCT
4401 AATCCTGTTA CCAGTGGCTG CTGCCAGTGG CGATAAGTCG
TGTCTTACCG
4451 GGTTGGACTC AAGACGATAG TTACCGGATA AGGCGCAGCG
GTCGGGCTGA

4501 ACGGGGGGTT CGTGCACACA GCCCAGCTTG GAGCGAACGA
CCTACACCGA
4551 ACTGAGATAC CTACAGCGTG AGCTATGAGA AAGCGCCACG
CTTCCCGAAG
4601 GGAGAAAGGC GGACAGGTAT CCGGTAAGCG GCAGGGTCGG
AACAGGAGAG
4651 CGCACGAGGG AGCTTCCAGG GGGAAACGCC TGGTATCTTT
ATAGTCCTGT
4701 CGGGTTTCGC CACCTCTGAC TTGAGCGTCG ATTTTTGTGA
TGCTCGTCAG
4751 GGGGGCGGAG CCTATGGAAA AACGCCAGCA ACGCGGCCTT
TTTACGGTTC
4801 CTGGCCTTTT GCTGGCCTTT TGCTCACATG TTCTTTCCTG
CGTTATCCCC
4851 TGATTCTGTG GATAACCGTA TTACCGCCTT TGAGTGAGCT
GATACCGCTC
4901 GCCGCAGCCG AACGACCGAG CGCAGCGAGT CAGTGAGCGA
GGAAGCGGAA
4951 GAGCGCCCAA TACGCAAACC GCCTCTCCCC GCGCGTTGGC
CGATTCATTA
5001 ATGCAGCTGG CACGACAGGT TTCCCGACTG GAAAGCGGGC
AGTGAGCGCA
5051 ACGCAATTAA TGTGAGTTAG CTCACTCATT AGGCACCCCA
GGCTTTACAC
5101 TTTATGCTTC CGGCTCGTAT GTTGTGTGGA ATTGTGAGCG
GATAACAATT
5151 TCACACAGGA AACAGCTATG ACCATGATTA CGCCAAGCTA
TTTAGGTGAC
5201 ACTATAGAAT ACTCAAGCTT TCTAGATTAA GG

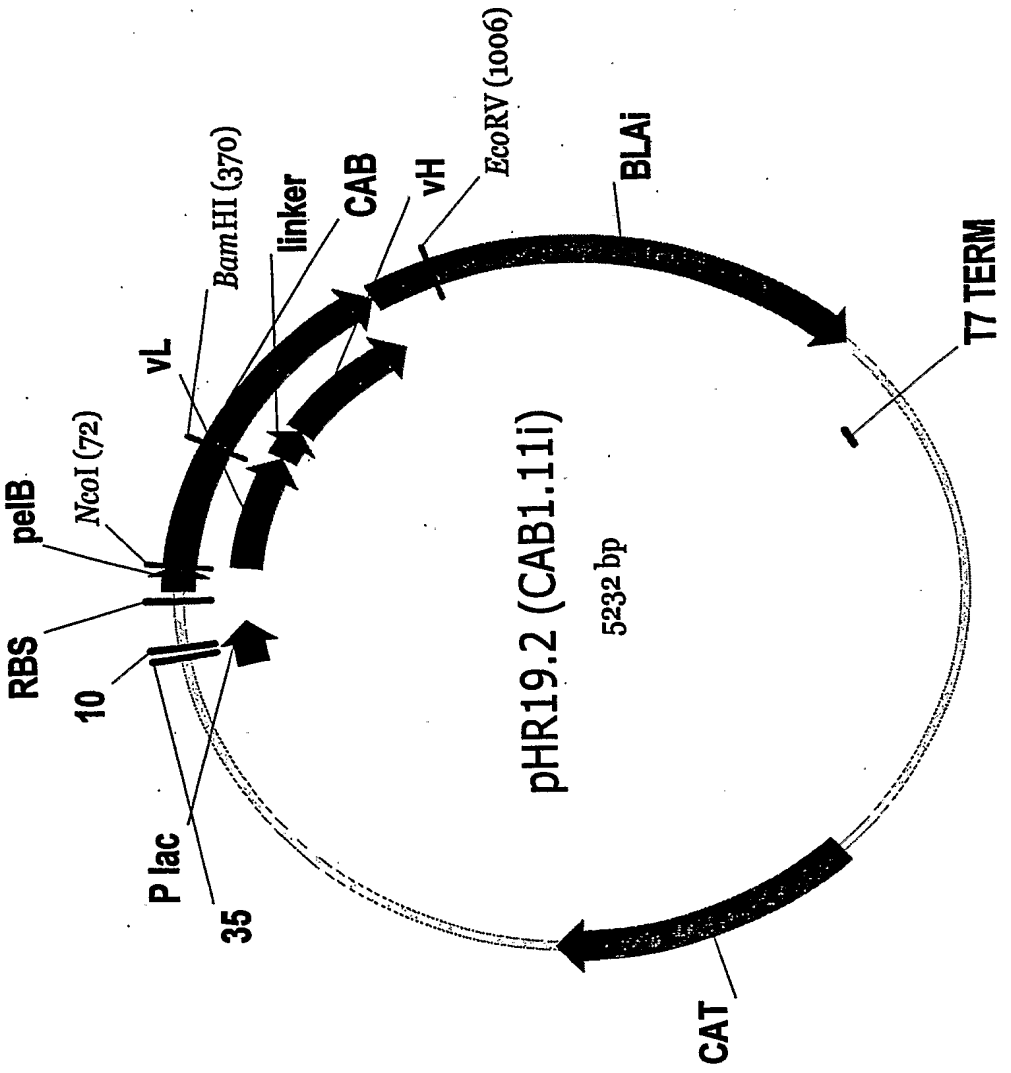

pHR19.2 (CAB1.11i)
5232 bp
P lac
35
RBS
10
pelB
NcoI (72)
vL
BamHI (370)
linker
CAB
vH
EcoRV (1006)
BLAi
T7 TERM
CAT

Figure 5

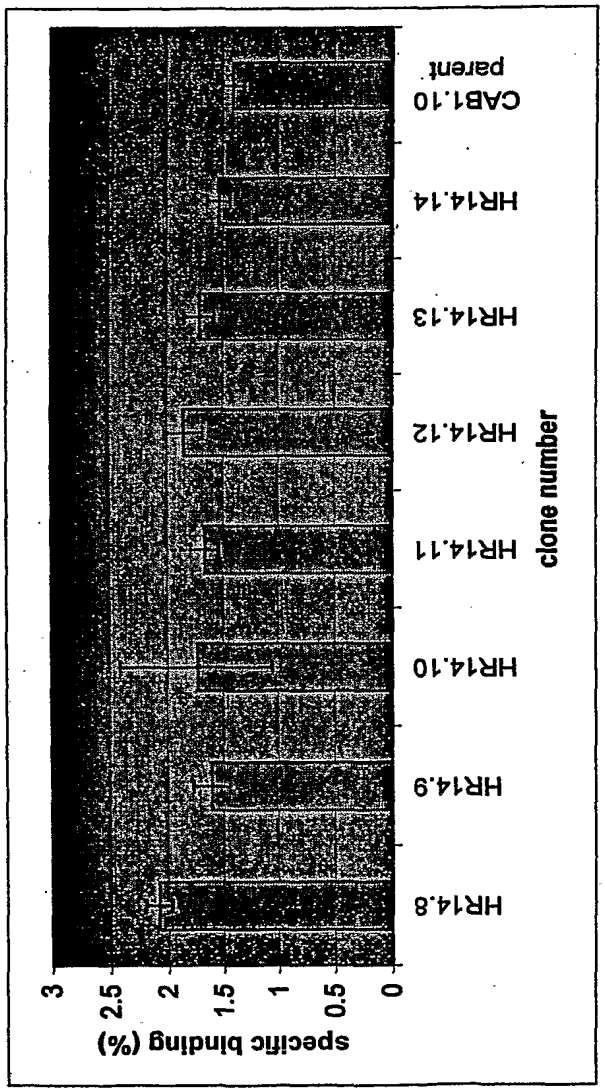
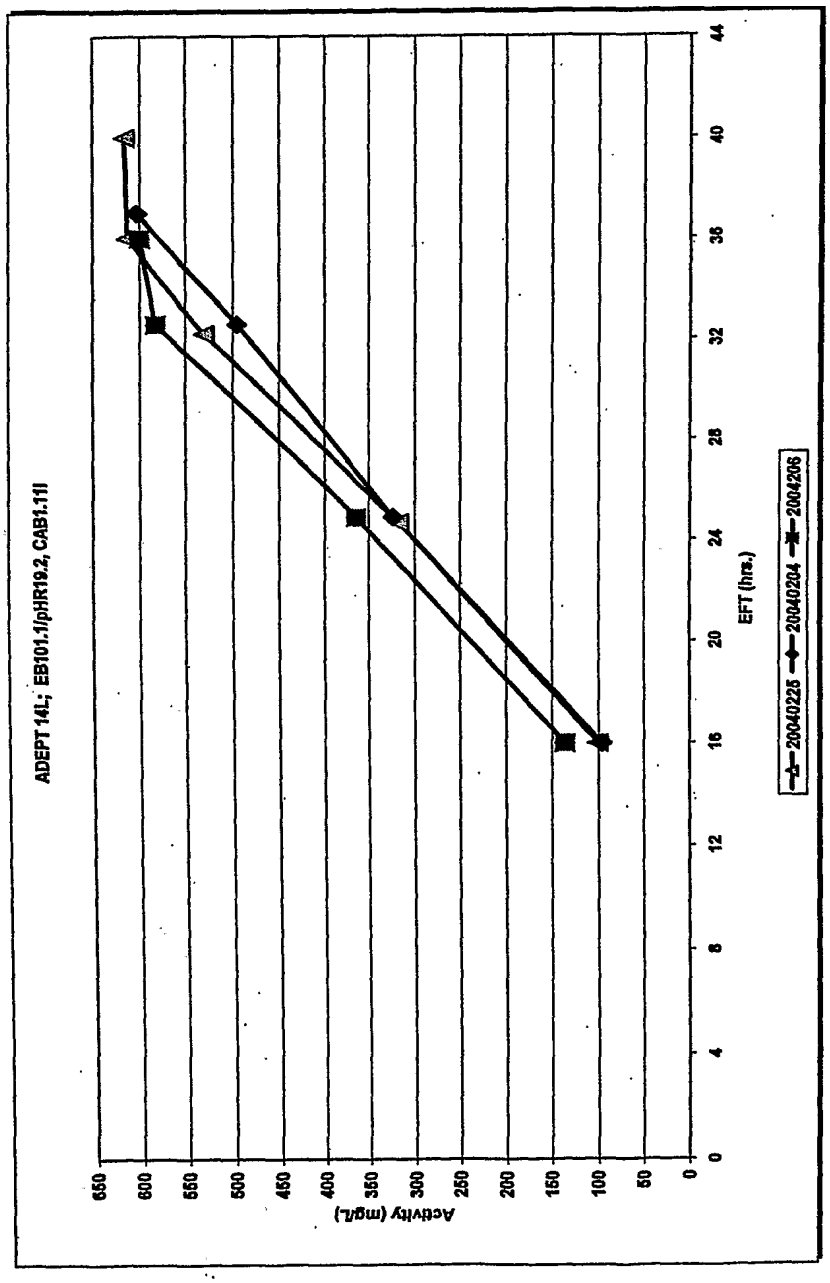

specific binding (%)
0
0.5
1
1.5
2
2.5
3
clone number
HR14.8
HR14.9
HR14.10
HR14.11
HR14.12
HR14.13
HR14.14
CAB1.10
parent

Figure 6

Figure 7


ADEPT 14L; EB101.1/pHR19.2, CAB1.11I
Activity (mg/L)
EFT (hrs.)
20040225
20040304
20040306

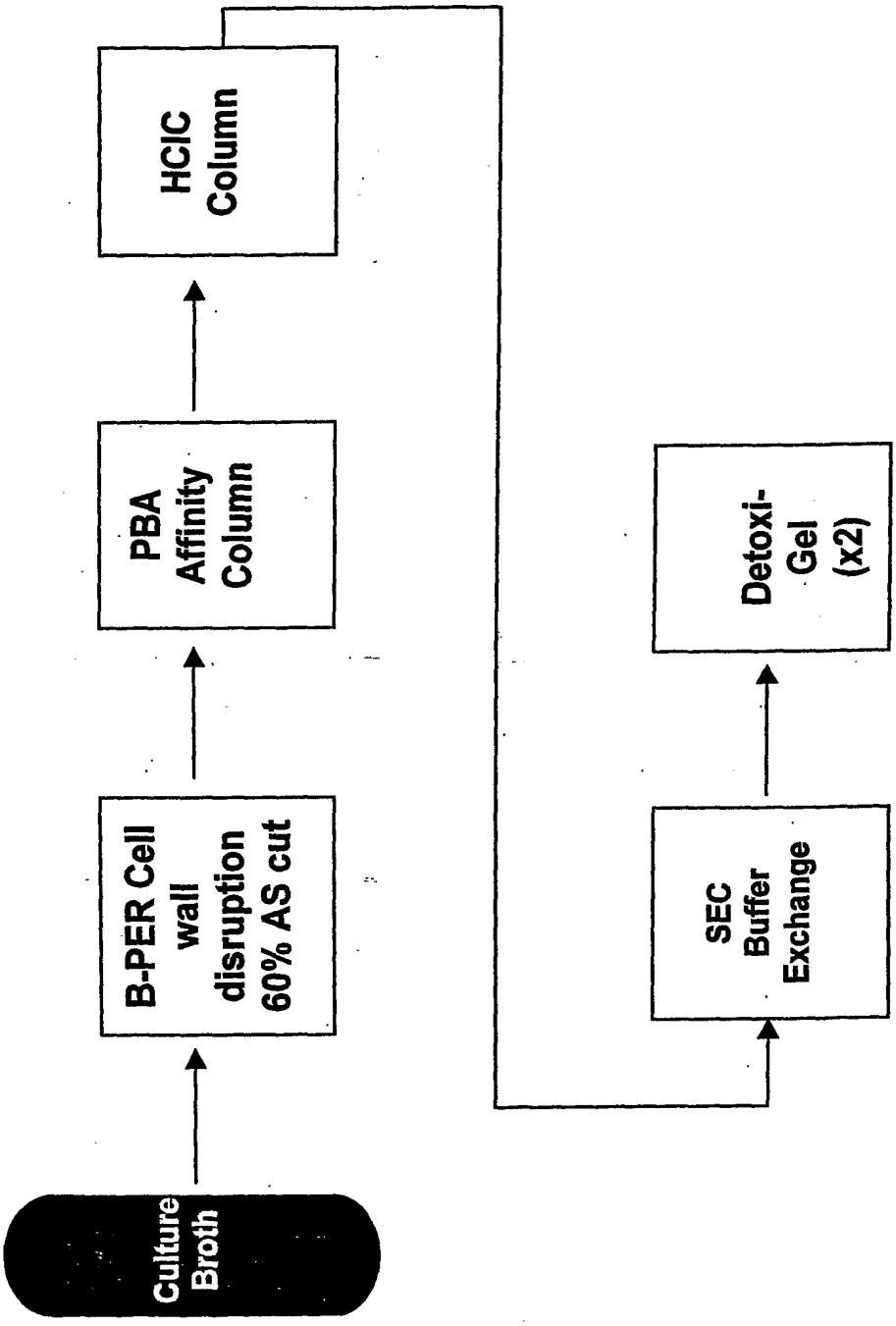

Culture Broth
B-PER Cell wall disruption 60% AS cut
PBA Affinity Column
HCIC Column
Detoxi-Gel (x2)
SEC Buffer Exchange

Figure 8

Figure 9

Lane 1: molecular weight standard; Lanes 3-5: unrelated proteins; lane 6: CAB1.11i.

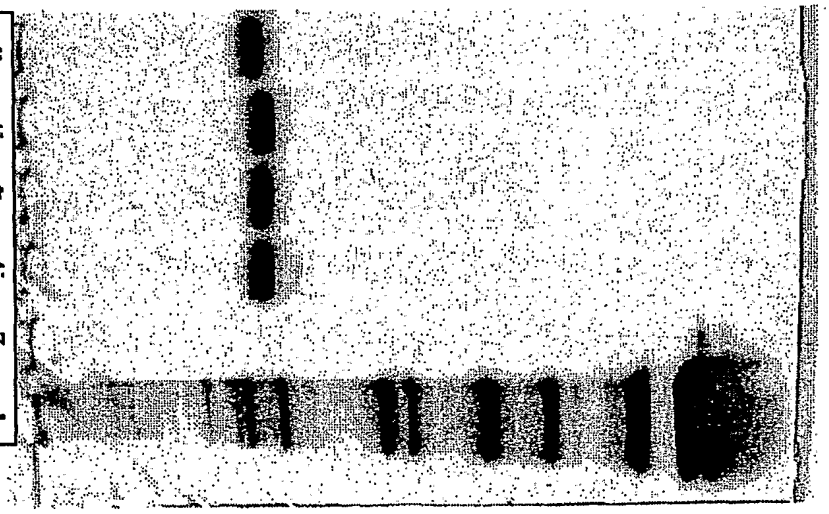


Figure 10A

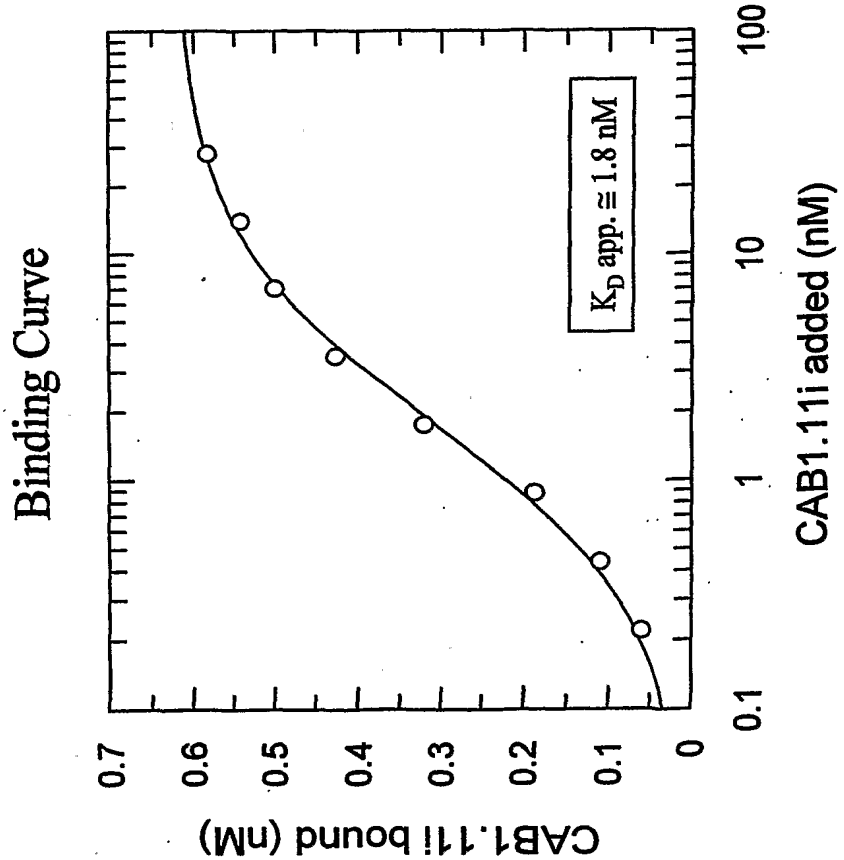


Figure 10B

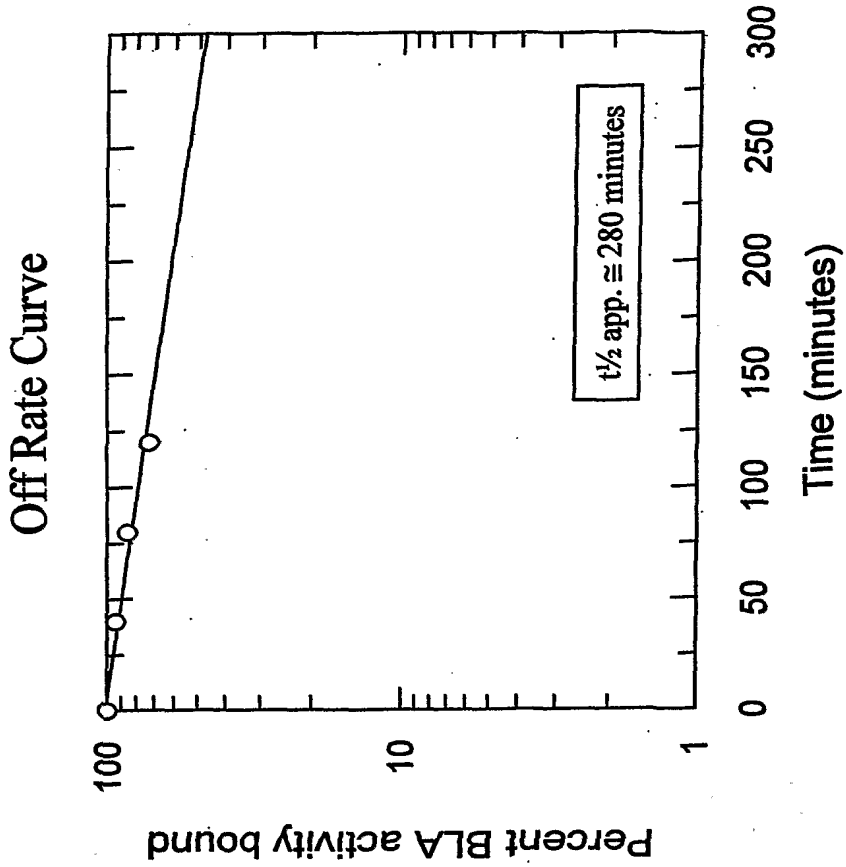
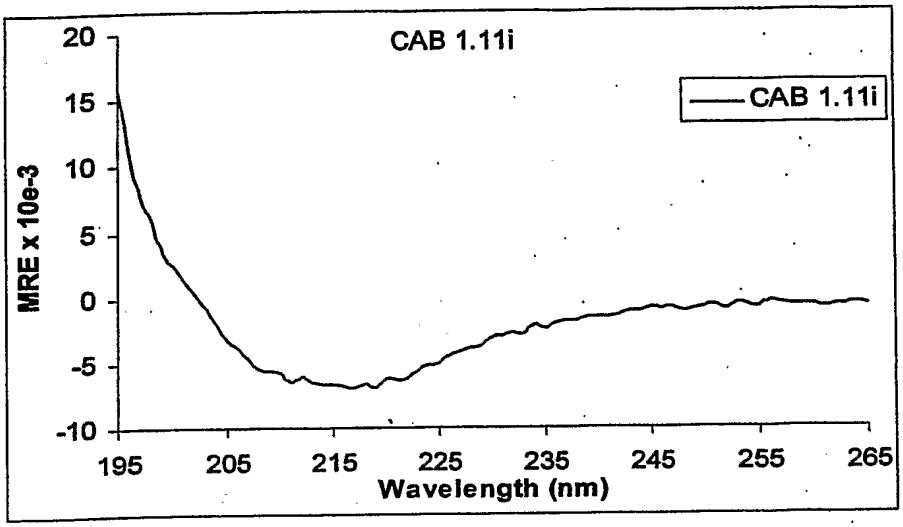


Figure 11


CAB 1.11i
CAB 1.11i
MRE x 10e-3
20
15
10
5
0
-5
-10
195
205
215
225
235
245
255
265
Wavelength (nm)

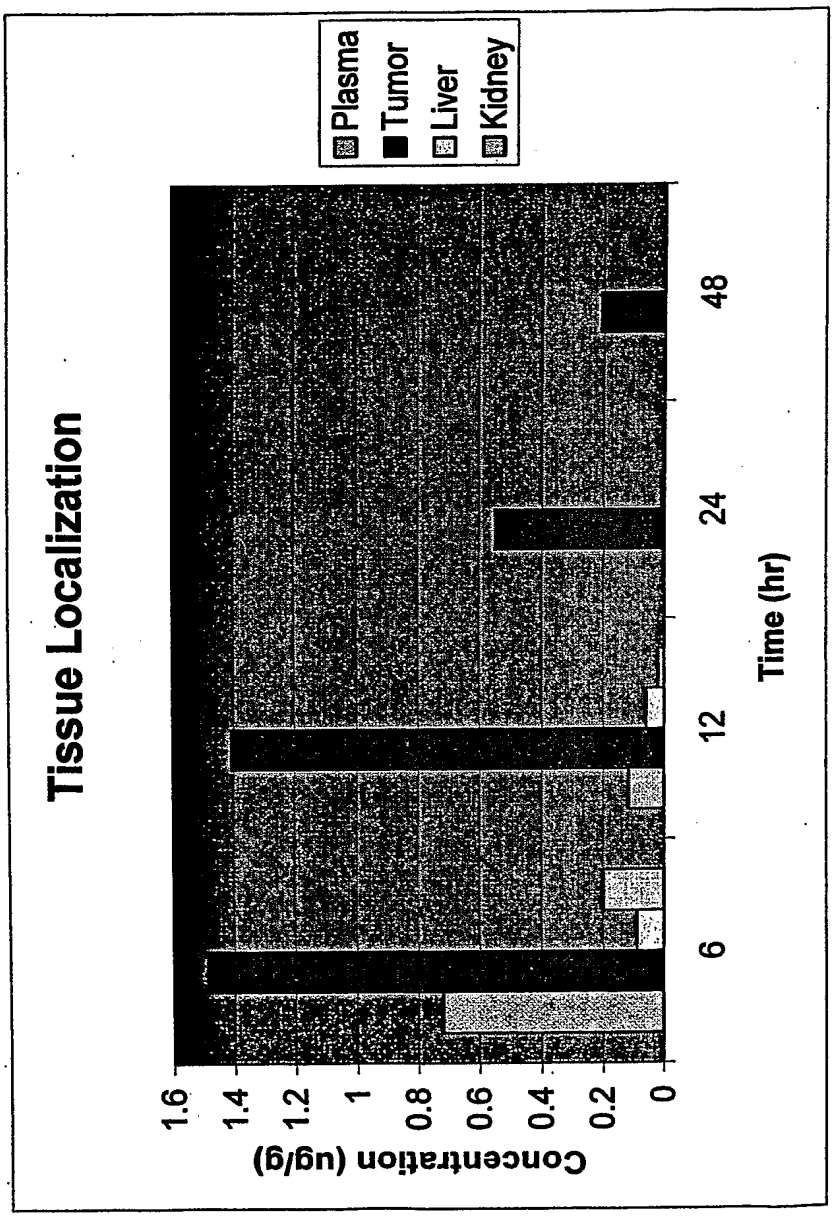

Tissue Localization
Plasma
Tumor
Liver
Kidney
Concentration (ug/g)
0
0.2
0.4
0.6
0.8
1
1.2
1.4
1.6
6
12
24
48
Time (hr)

Figure 12

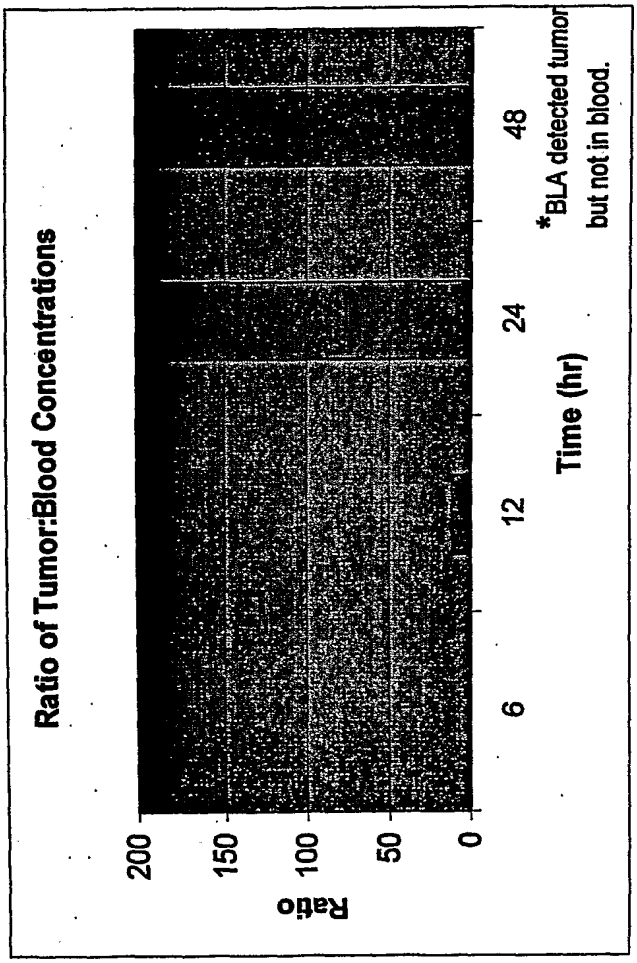

Ratio of Tumor:Blood Concentrations
Ratio
200
150
100
50
0
6
12
24
48
Time (hr)
*BLA detected tumor but not in blood.

Figure 13

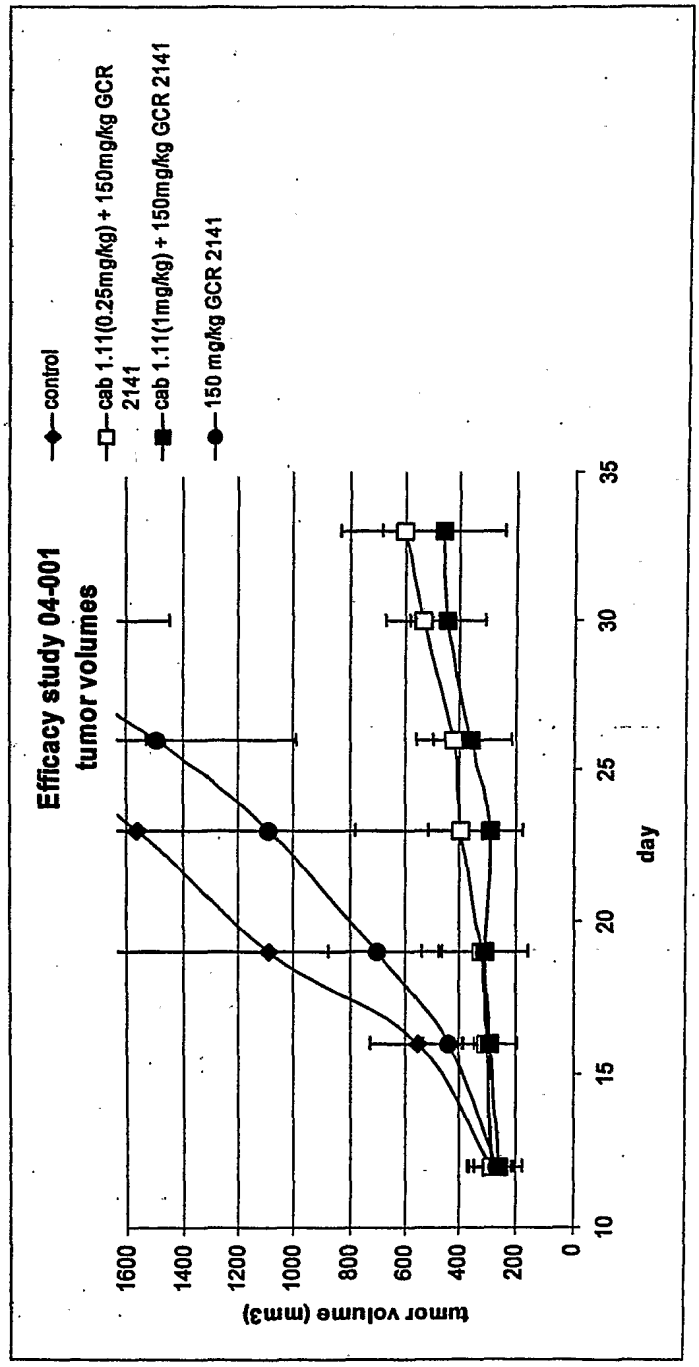

Efficacy study 04-001
tumor volumes
control
cab 1.11(0.25mg/kg) + 150mg/kg GCR 2141
cab 1.11(1mg/kg) + 150mg/kg GCR 2141
150 mg/kg GCR 2141
tumor volume (mm3)
1600
1400
1200
1000
800
600
400
200
0
10
15
20
25
30
35
day

Figure 14

Case ID	ASM	Sample ID	Sample Pathology
CI0000000255	DF5	FR00005C7B	Adenocarcinoma of lung
CI0000005496	FF5	FR5B337147	Adenocarcinoma of lung
CI0000011577	FF1	FR5B34059F	Adenocarcinoma of lung
CI7000000241	AF4	FR0003A78	Adenocarcinoma of lung [redacted]
CI0000007518	AF5	FR0001FD15	Carcinoma of lung, squamous cell
CI0000008475	IF4	FR65EE0784	Adenocarcinoma of colon, metastatic
CI0000015252	FF2	FR5B342166	Adenocarcinoma of colon

FIGURE 15-A

Case Diagnosis	Tissue of Origin/Site of Finding	H/E	Anti-H
Adenocarcinoma of lung Grade: AJCC G3: Poorly differentiated Stage: IIIA	Lung/Lung	4X 20X	Immunoger 4x
Adenocarcinoma of lung Grade: AJCC G3: Poorly differentiated Stage: IIIB	Lung/Lung	4X 20X	
Adenocarcinoma of lung Grade: AJCC G2: Moderately differentiated Stage: IIIA	Lung/Lung	4X 20X	
Adenocarcinoma of lung Grade: AJCC G2: Moderately differentiated Stage: IIIA	Lung/Lung	4X 20X	
Carcinoma of lung, squamous cell Grade: AJCC G3: Poorly differentiated Stage: IIIA	Lung/Lung	4X 20X	
Adenocarcinoma of colon, metastatic Grade: Not Reported Stage: IV	Colon/Liver	4X 20X	4x
Adenocarcinoma of colon Grade: AJCC G3: Poorly differentiated Stage: IIIB	Cecum/Cecum	4X 20X	

FIG. 15-A

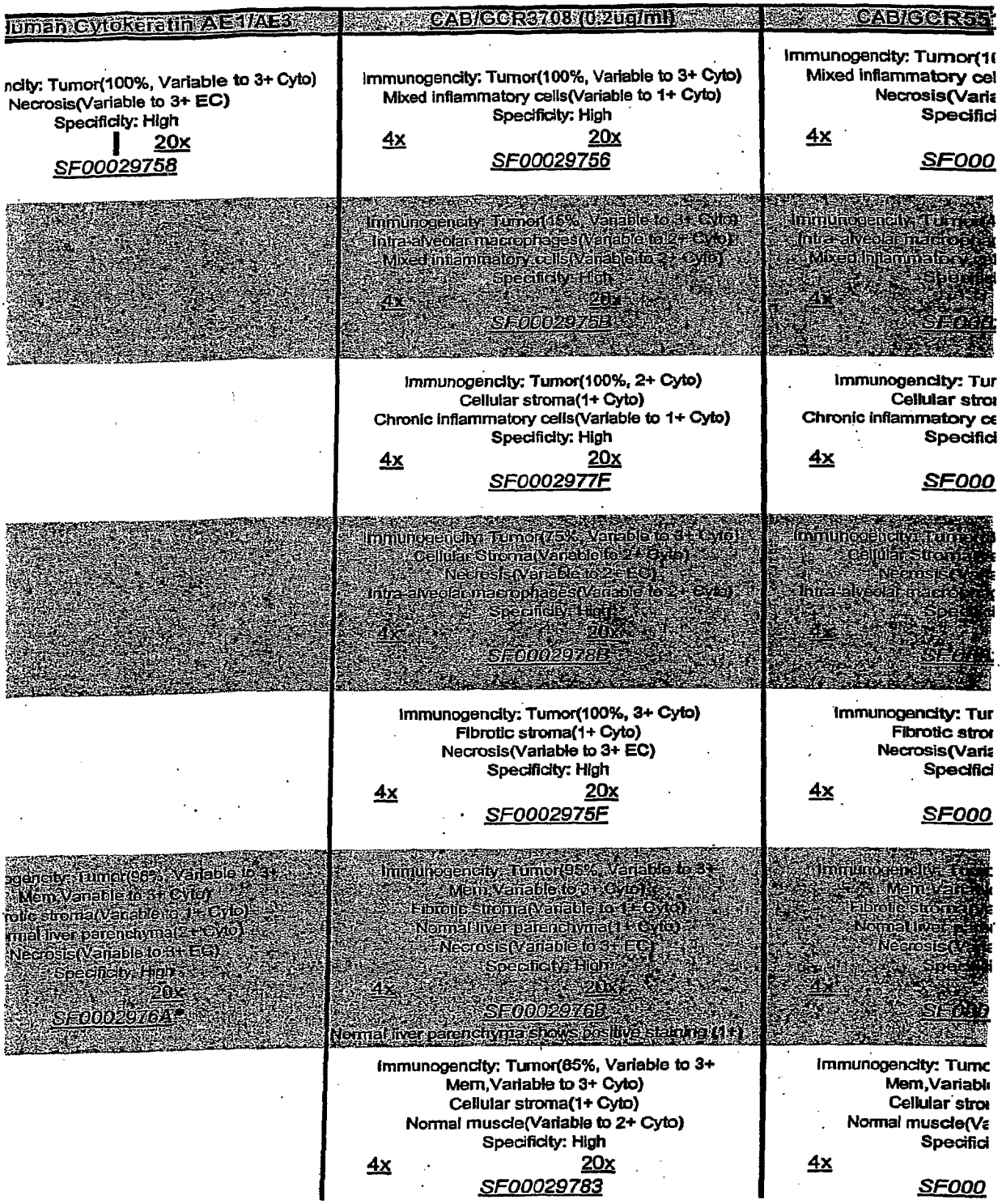

Human Cytokeratin AE1/AE3
CAB/CGR3708 (0.2ug/ml)
CAB/CGR55
ncity: Tumor(100%, Variable to 3+ Cyto)
Necrosis(Variable to 3+ EC)
Specificity: High
20x
SF00029758
Immunogencity: Tumor(100%, Variable to 3+ Cyto)
Mixed inflammatory cells(Variable to 1+ Cyto)
Specificity: High
4x
20x
SF00029756
Immunogencity: Tumor(
Mixed inflammatory cel
Necrosis(Varia
Specifici
4x
SF000
Immunogencity: Tumor(15%, Variable to 3+ Cyto)
Intra-alveolar macrophages(Variable to 2+ Cyto)
Mixed inflammatory cells(Variable to 2+ Cyto)
Specificity: High
4x
20x
SF0002975B
Immunogencity: Tumor(100%, 2+ Cyto)
Cellular stroma(1+ Cyto)
Chronic inflammatory cells(Variable to 1+ Cyto)
Specificity: High
4x
20x
SF0002977F
Immunogencity: Tur
Cellular stro
Chronic inflammatory ce
Specifici
4x
SF000
Immunogencity: Tumor(75%, Variable to 3+ Cyto)
Cellular Stroma(Variable to 2+ Cyto)
Necrosis(Variable to 2+ EC)
Intra-alveolar macrophages(Variable to 2+ Cyto)
Specificity: High
4x
20x
SF0002978B
Immunogencity: Tumor(100%, 3+ Cyto)
Fibrotic stroma(1+ Cyto)
Necrosis(Variable to 3+ EC)
Specificity: High
4x
20x
SF0002975F
Immunogencity: Tur
Fibrotic stro
Necrosis(Varia
Specifici
4x
SF000
ogencity: Tumor(95%, Variable to 3+
Mem,Variable to 3+ Cyto)
rotic stroma(Variable to 1+ Cyto)
rmal liver parenchyma(1+ Cyto)
Necrosis(Variable to 3+ EC)
Specificity: High
20x
SF00029764
Immunogencity: Tumor(95%, Variable to 3+
Mem,Variable to 3+ Cyto)
Fibrotic stroma(Variable to 1+ Cyto)
Normal liver parenchyma(1+ Cyto)
Necrosis(Variable to 3+ EC)
Specificity: High
4x
20x
SF00029768
Normal liver parenchyma shows positive staining (1+)
Immunogencity: Tumor(65%, Variable to 3+
Mem,Variable to 3+ Cyto)
Cellular stroma(1+ Cyto)
Normal muscle(Variable to 2+ Cyto)
Specificity: High
4x
20x
SF00029783
Immunogencity: Tumo
Mem,Variabl
Cellular stro
Normal muscle(Va
Specifici
4x
SF000

FIG. 15C

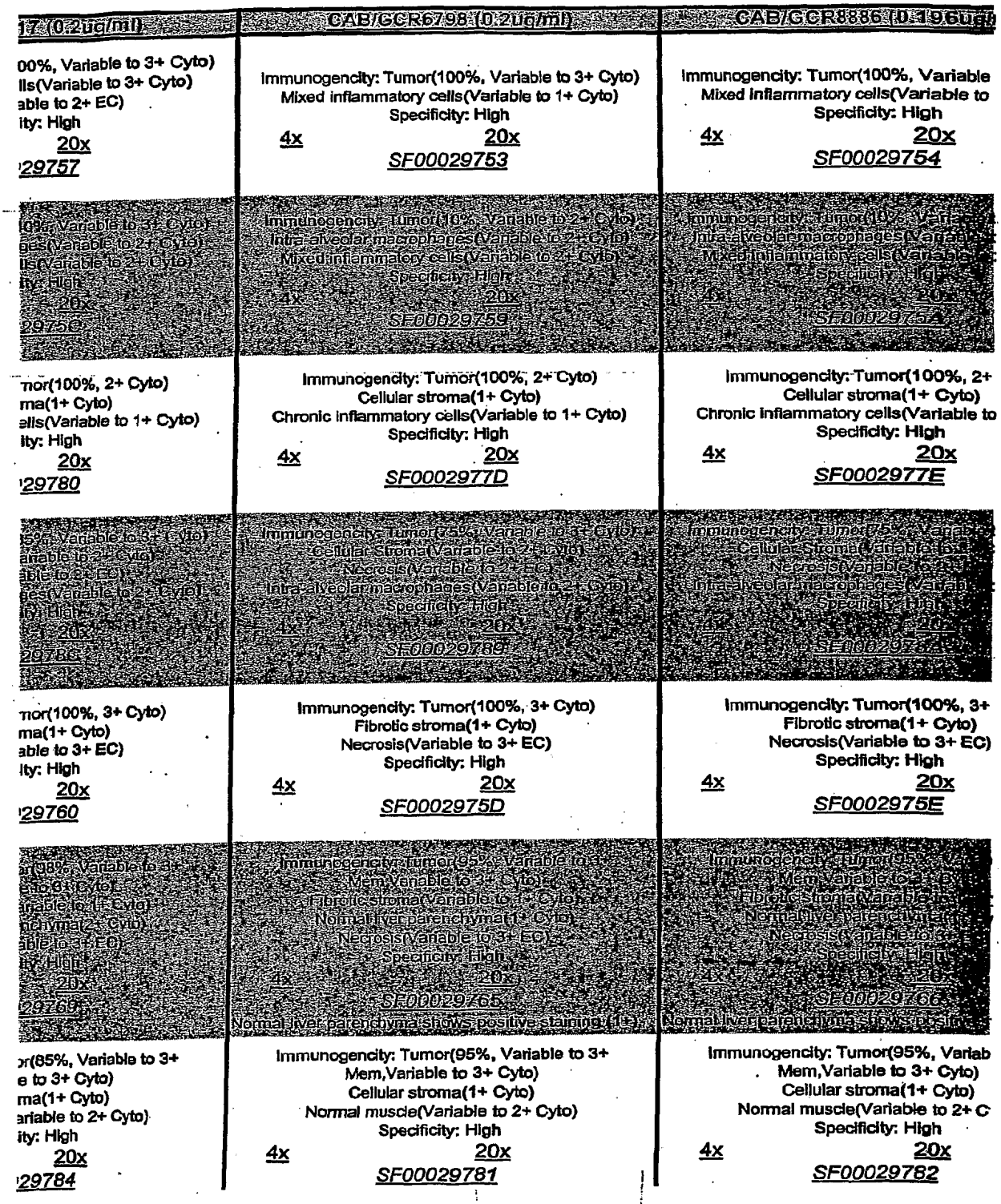

17 (0.2ug/ml)
CAB/GCR6798 (0.2ug/ml)
CAB/GCR8886 (0.196ug/
00%, Variable to 3+ Cyto)
lls(Variable to 3+ Cyto)
able to 2+ EC)
ity: High
20x
29757
Immunogenicity: Tumor(100%, Variable to 3+ Cyto)
Mixed inflammatory cells(Variable to 1+ Cyto)
Specificity: High
4x
20x
SF00029753
Immunogenicity: Tumor(100%, Variable
Mixed inflammatory cells(Variable to
Specificity: High
4x
20x
SF00029754
20x
29758
Immunogenicity: Tumor(100%, Variable to 2+ Cyto)
Intra-alveolar macrophages(Variable to 2+ Cyto)
Mixed inflammatory cells(Variable to 2+ Cyto)
Specificity: High
4x
20x
SF00029759
nor(100%, 2+ Cyto)
ma(1+ Cyto)
ells(Variable to 1+ Cyto)
ity: High
20x
29780
Immunogenicity: Tumor(100%, 2+ Cyto)
Cellular stroma(1+ Cyto)
Chronic inflammatory cells(Variable to 1+ Cyto)
Specificity: High
4x
20x
SF0002977D
Immunogenicity: Tumor(100%, 2+
Cellular stroma(1+ Cyto)
Chronic inflammatory cells(Variable to
Specificity: High
4x
20x
SF0002977E
20x
29786
Immunogenicity: Tumor(95%, Variable to 3+ Cyto)
Cellular stroma(Variable to 2+ Cyto)
Necrosis(Variable to 2+ EC)
Intra-alveolar macrophages(Variable to 2+ Cyto)
Specificity: High
4x
20x
SF00029789
nor(100%, 3+ Cyto)
ma(1+ Cyto)
able to 3+ EC)
ity: High
20x
29760
Immunogenicity: Tumor(100%, 3+ Cyto)
Fibrotic stroma(1+ Cyto)
Necrosis(Variable to 3+ EC)
Specificity: High
4x
20x
SF0002975D
Immunogenicity: Tumor(100%, 3+
Fibrotic stroma(1+ Cyto)
Necrosis(Variable to 3+ EC)
Specificity: High
4x
20x
SF0002975E
20x
29760
Immunogenicity: Tumor(95%, Variable to 3+
Mem,Variable to 3+ Cyto)
Fibrotic stroma(Variable to 1+ Cyto)
Normal liver parenchyma(1+ Cyto)
Necrosis(Variable to 3+ EC)
Specificity: High
4x
20x
SF00029765
Normal liver parenchyma shows positive staining (1+)
Immunogenicity: Tumor(95%, Variable to 3+
Mem,Variable to 3+ Cyto)
Fibrotic stroma(Variable to 1+ Cyto)
Normal liver parenchyma(1+ Cyto)
Necrosis(Variable to 3+ EC)
Specificity: High
4x
20x
SF00029766
Normal liver parenchyma shows positive
or(85%, Variable to 3+
e to 3+ Cyto)
ma(1+ Cyto)
ariable to 2+ Cyto)
ity: High
20x
29784
Immunogenicity: Tumor(95%, Variable to 3+
Mem,Variable to 3+ Cyto)
Cellular stroma(1+ Cyto)
Normal muscle(Variable to 2+ Cyto)
Specificity: High
4x
20x
SF00029781
Immunogenicity: Tumor(95%, Variab
Mem,Variable to 3+ Cyto)
Cellular stroma(1+ Cyto)
Normal muscle(Variable to 2+ C
Specificity: High
4x
20x
SF00029782

FIG. 15-D

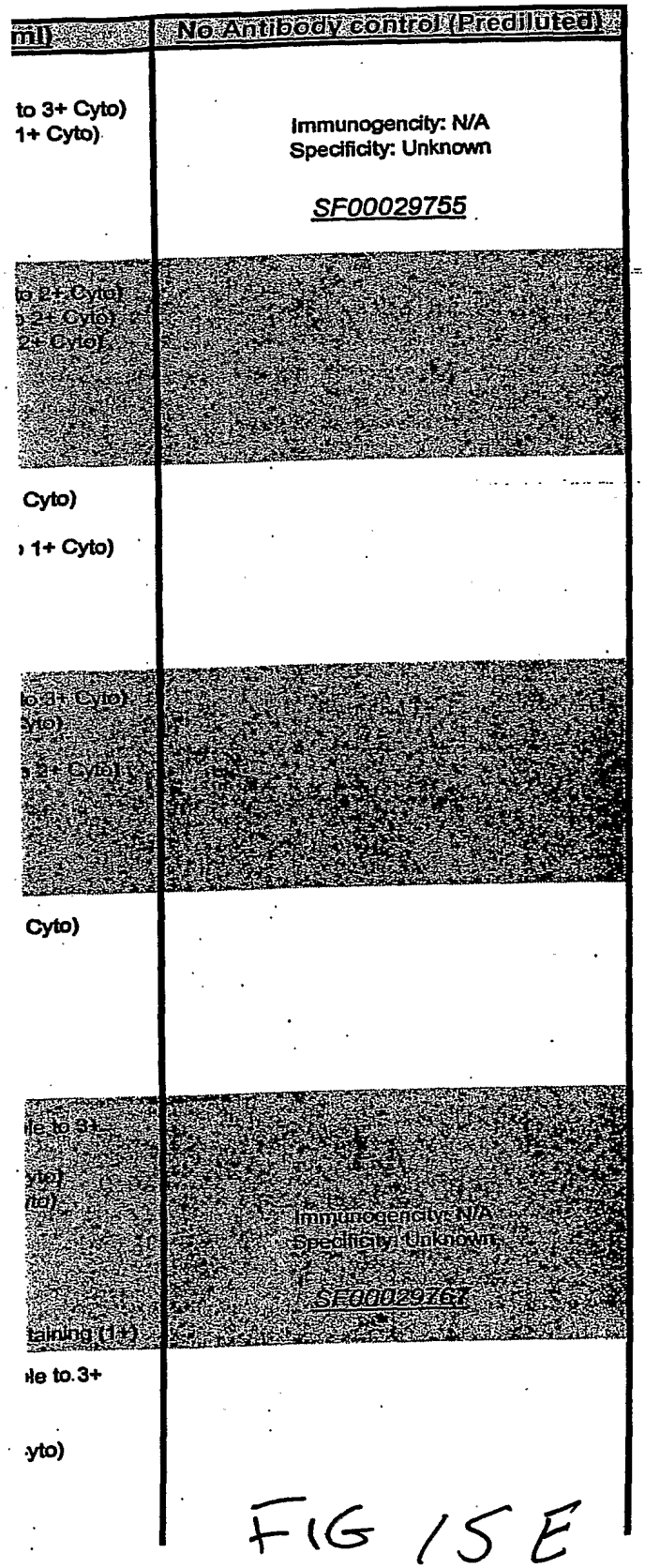

ml)
No Antibody control (Prediluted)
to 3+ Cyto)
1+ Cyto)
Immunogencity: N/A
Specificity: Unknown
SF00029755
Cyto)
1+ Cyto)
Cyto)
Immunogencity: N/A
Specificity: Unknown
SF00029767
staining (1+)
le to 3+
yto)

FIG 15E

CI0000017970	HF1	FR65EE7B3D	Adenocarcinoma of colon
CI0000010013	AF2	FR00028F2E	Adenocarcinoma of pancreas, metastatic
CI0000009651	AF1	FR0002B111	Adenocarcinoma of pancreas, ductal
CI0000008690	CF4	FR00027B0E	Adenocarcinoma of pancreas, ductal
CI0000007678	AF3	FR0002575B	Adenocarcinoma of pancreas, ductal
CI0000009736	AF2	FR0002BAB4	Adenocarcinoma of pancreas, ductal

FIG. 15-F

Adenocarcinoma of colon Grade: AJCC G2: Moderately differentiated Stage: IIIC	Colon/Colon	4X 20X	
Adenocarcinoma of pancreas, metastatic Grade: Not Reported Stage: IV	Pancreas/Omentum	4X 20X	Immu Fibro 4x
Adenocarcinoma of pancreas, ductal Grade: AJCC G2: Moderately differentiated Stage: IIB	Pancreas/Pancreas	4X 20X	
Adenocarcinoma of pancreas, ductal Grade: AJCC G1: Well differentiated Stage: IIA	Pancreas/Pancreas	4X 20X	
Adenocarcinoma of pancreas, ductal Grade: AJCC G2: Moderately differentiated Stage: III	Pancreas/Pancreas	4X 20X	
Adenocarcinoma of pancreas, ductal Grade: AJCC G2: Moderately differentiated Stage: IIB	Pancreas/Pancreas	4X 20X	

FIG.

15-G

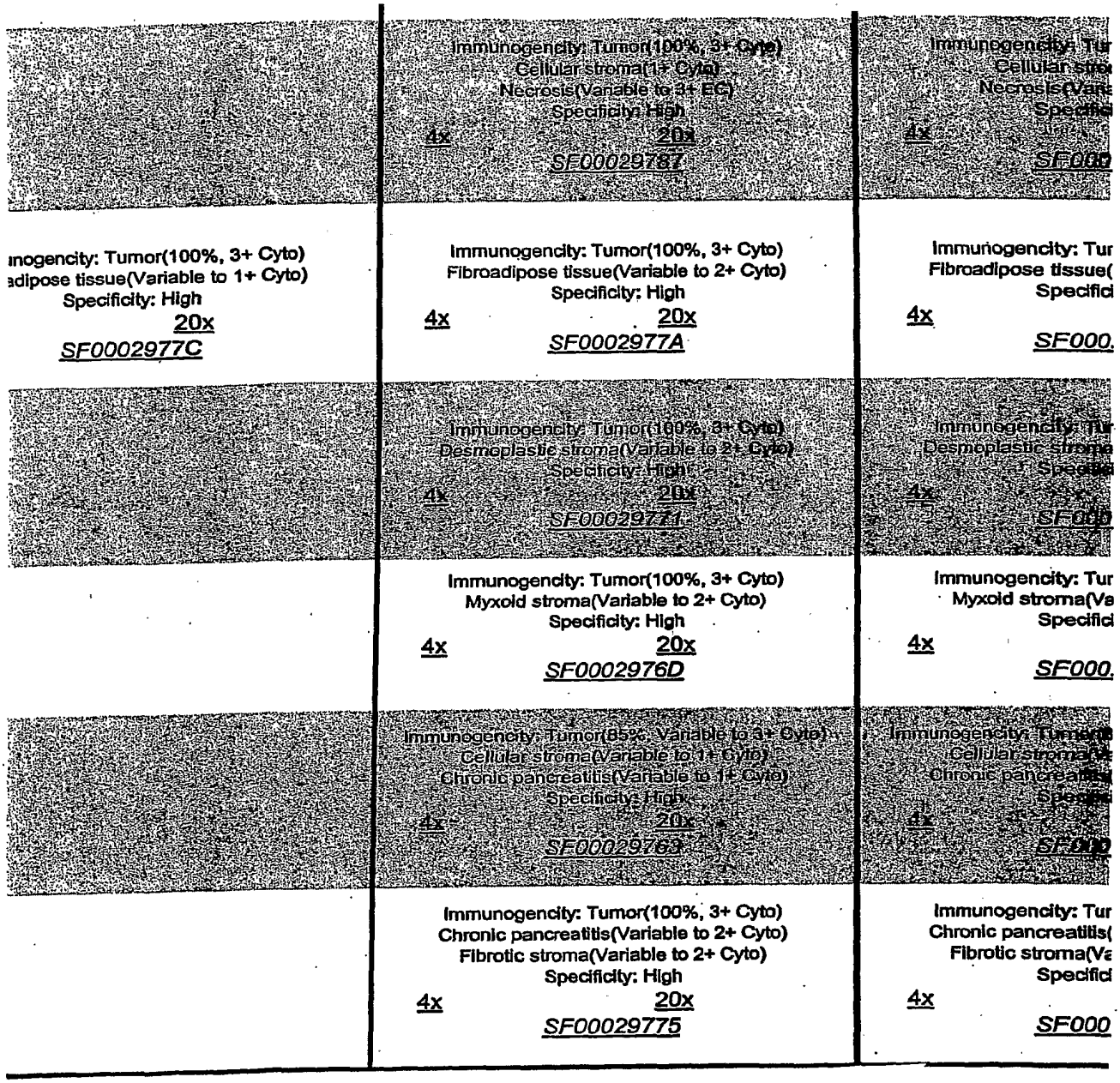

Immunogencity: Tumor(100%, 3+ Cyto)
Cellular stroma(1+ Cyto)
Necrosis(Variable to 3+ EC)
Specificity: High
4x
20x
SF00029787
Immunogencity: Tumor(100%, 3+ Cyto)
Fibroadipose tissue(Variable to 1+ Cyto)
Specificity: High
20x
SF0002977C
Immunogencity: Tumor(100%, 3+ Cyto)
Fibroadipose tissue(Variable to 2+ Cyto)
Specificity: High
4x
20x
SF0002977A
Immunogencity: Tumor(100%, 3+ Cyto)
Desmoplastic stroma(Variable to 2+ Cyto)
Specificity: High
4x
20x
SF00029771
Immunogencity: Tumor(100%, 3+ Cyto)
Myxoid stroma(Variable to 2+ Cyto)
Specificity: High
4x
20x
SF0002976D
Immunogencity: Tumor(85%, Variable to 3+ Cyto)
Cellular stroma(Variable to 1+ Cyto)
Chronic pancreatitis(Variable to 1+ Cyto)
Specificity: High
4x
20x
SF00029763
Immunogencity: Tumor(100%, 3+ Cyto)
Chronic pancreatitis(Variable to 2+ Cyto)
Fibrotic stroma(Variable to 2+ Cyto)
Specificity: High
4x
20x
SF00029775

FIG. 15-H

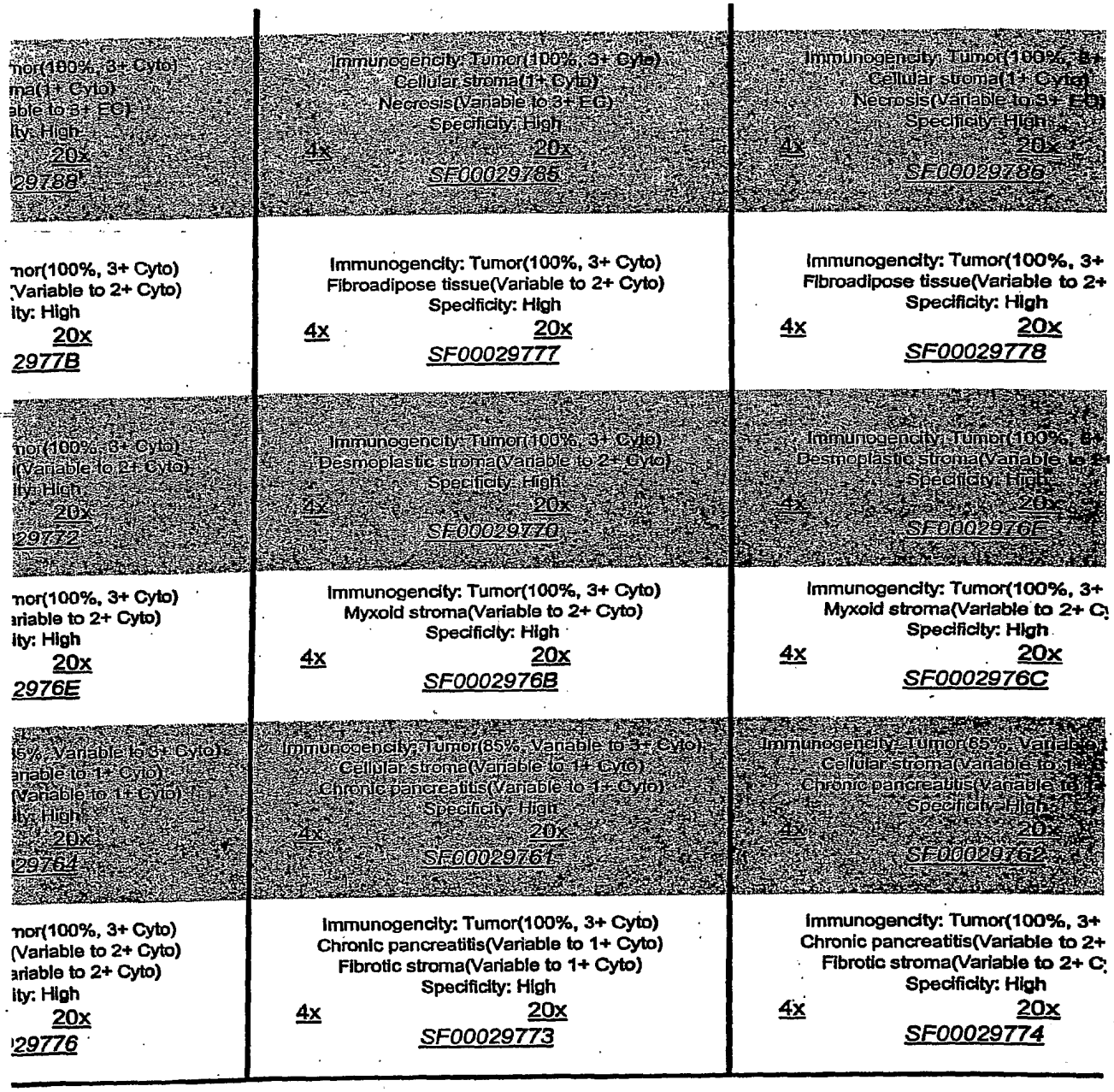

Immunogencity: Tumor(100%, 3+ Cyto)
Cellular stroma(1+ Cyto)
Necrosis(Variable to 3+ EC)
Specificity: High
4x
20x
SF00029785
Immunogencity: Tumor(100%, 3+
Cellular stroma(1+ Cyto)
Specificity: High
4x
20x
SF00029786
Immunogencity: Tumor(100%, 3+ Cyto)
Fibroadipose tissue(Variable to 2+ Cyto)
Specificity: High
4x
20x
SF00029777
Immunogencity: Tumor(100%, 3+
Fibroadipose tissue(Variable to 2+
Specificity: High
4x
20x
SF00029778
Immunogencity: Tumor(100%, 3+ Cyto)
Desmoplastic stroma(Variable to 2+ Cyto)
Specificity: High
4x
20x
SF00029770
Immunogencity: Tumor(100%, 3+
Desmoplastic stroma(Variable to
Specificity: High
4x
20x
SF0002976E
Immunogencity: Tumor(100%, 3+ Cyto)
Myxoid stroma(Variable to 2+ Cyto)
Specificity: High
4x
20x
SF0002976B
Immunogencity: Tumor(100%, 3+
Myxoid stroma(Variable to 2+ C
Specificity: High
4x
20x
SF0002976C
Immunogencity: Tumor(85%, Variable to 3+ Cyto)
Cellular stroma(Variable to 1+ Cyto)
Chronic pancreatitis(Variable to 1+ Cyto)
Specificity: High
4x
20x
SF00029761
Immunogencity: Tumor(65%, Variable
Cellular stroma(Variable to 1+
Chronic pancreatitis(Variable to 1+
Specificity: High
4x
20x
SF00029762
Immunogencity: Tumor(100%, 3+ Cyto)
Chronic pancreatitis(Variable to 1+ Cyto)
Fibrotic stroma(Variable to 1+ Cyto)
Specificity: High
4x
20x
SF00029773
Immunogencity: Tumor(100%, 3+
Chronic pancreatitis(Variable to 2+
Fibrotic stroma(Variable to 2+ C
Specificity: High
4x
20x
SF00029774

FIG.

15- I

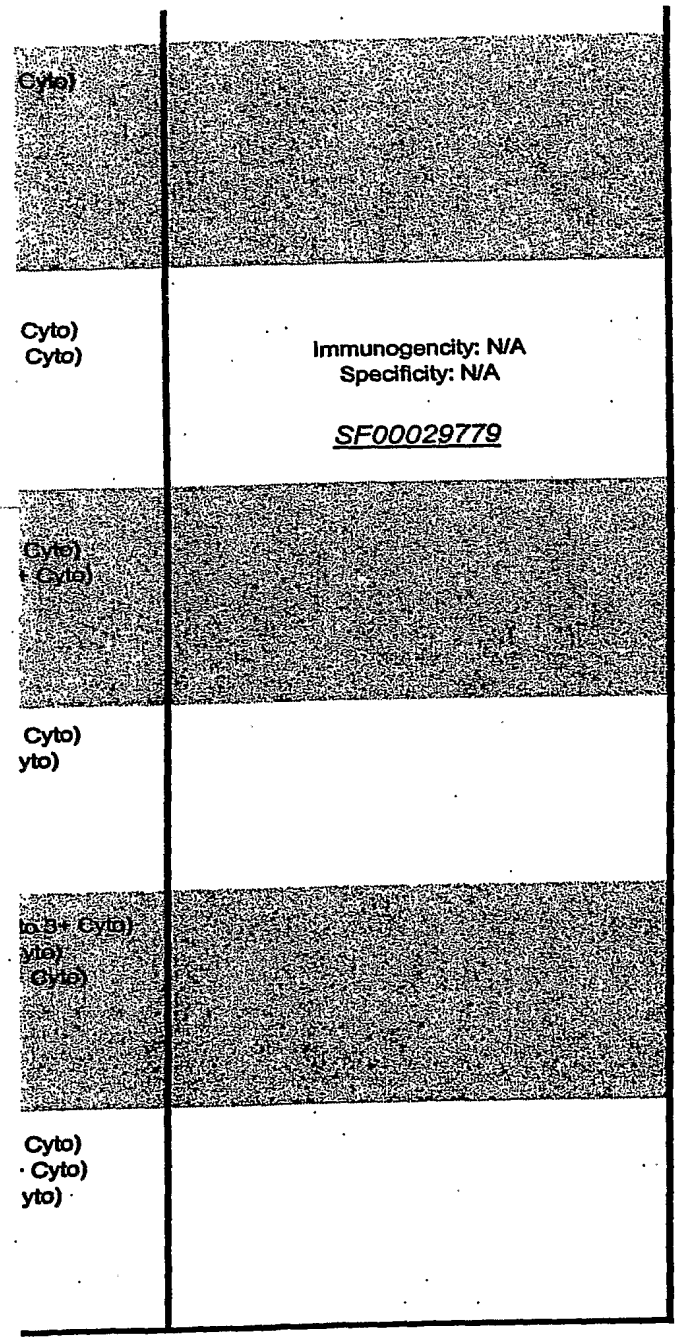

Cyto)
Cyto)
Cyto)
Immunogencity: N/A
Specificity: N/A
SF00029779
Cyto)
Cyto)
Cyto)
yto)
Cyto)
Cyto)
Cyto)
Cyto)
yto)

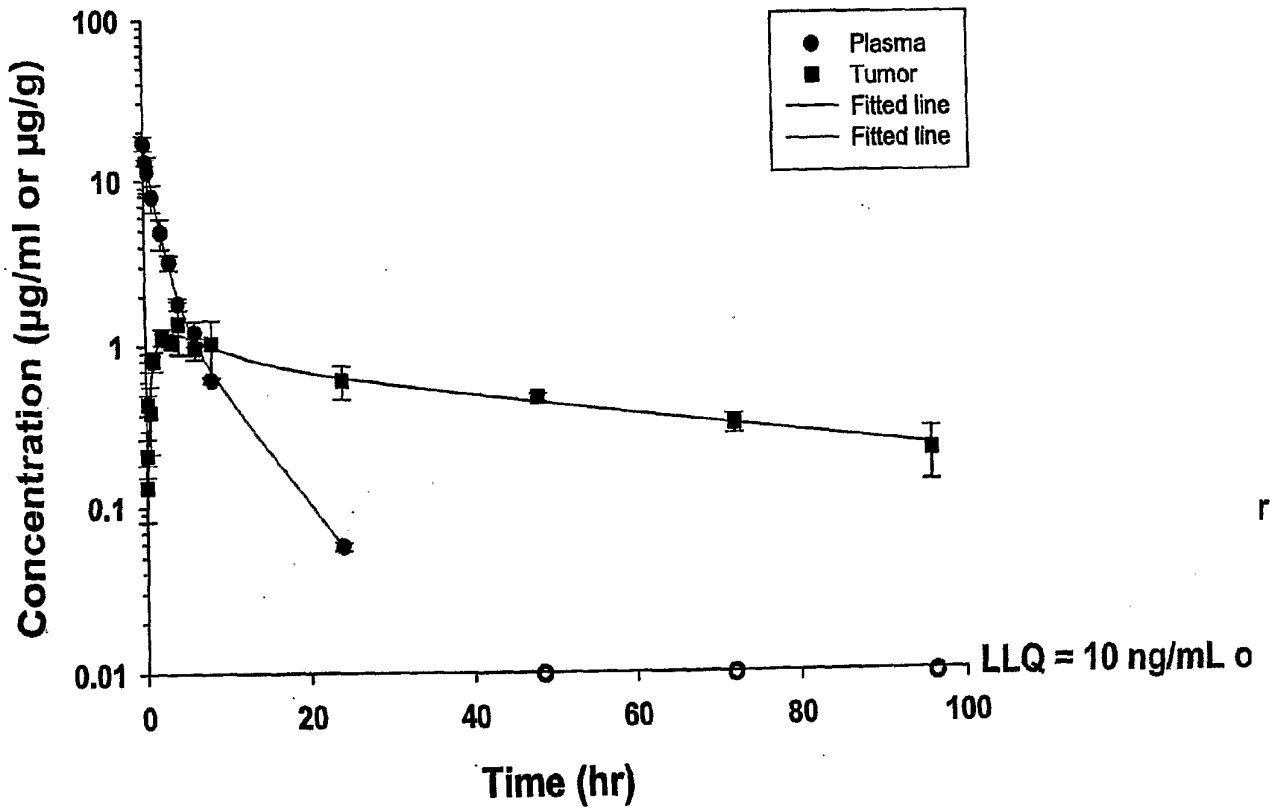
FIG. 15-J

CAB 1.11i FIG 164

Eliminated From Plasma and Retained in Tumor to At Least 96 hr

Plasma and tumor GCR-8886 concentration-time profiles (log-linear scale)

Fig 164



r g

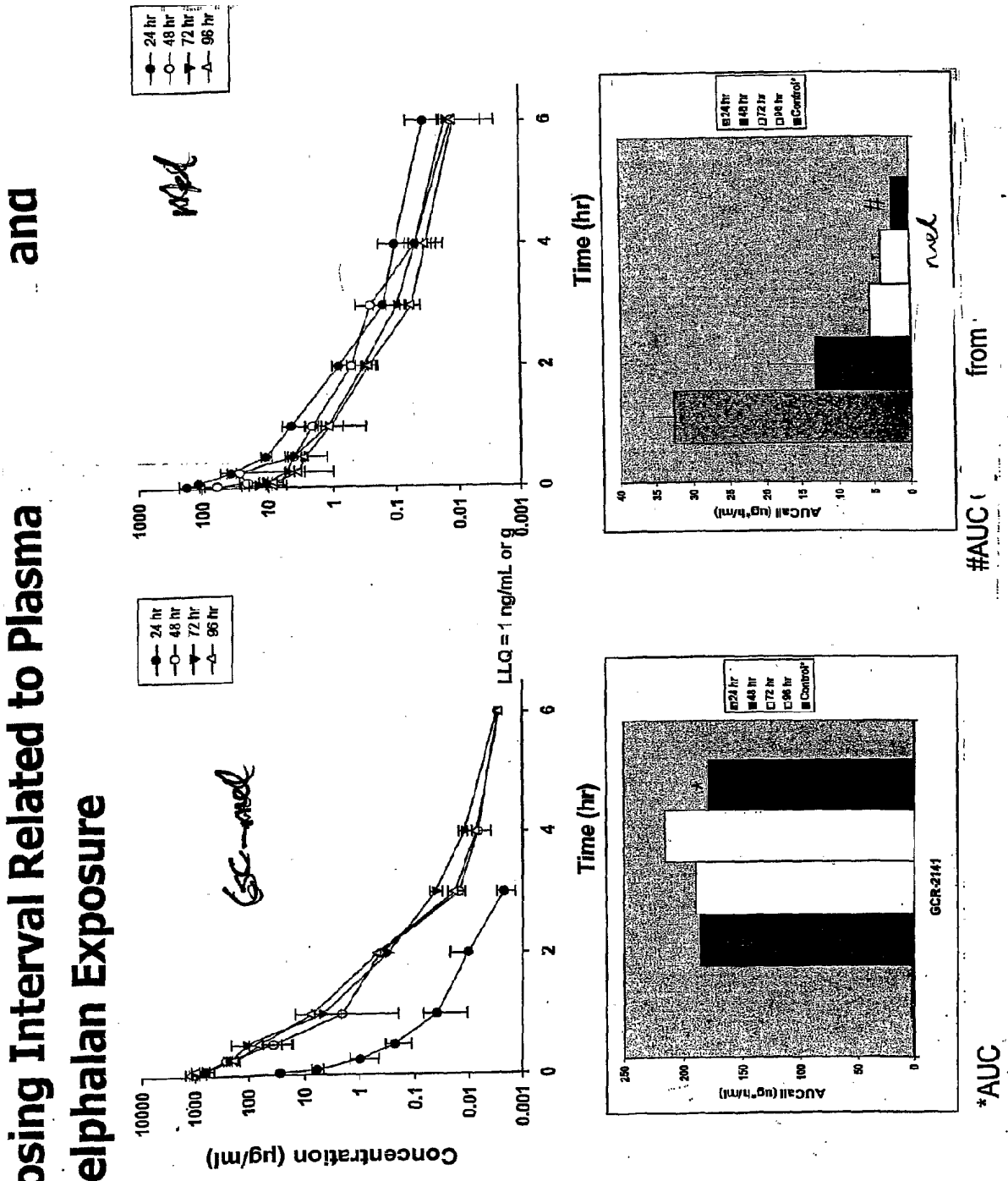

Dosing Interval Related to Plasma
Melphalan Exposure
and
24 hr
48 hr
72 hr
96 hr
Concentration (µg/ml)
LLQ = 1 ng/mL or g
Time (hr)
AUCall (ug*h/ml)
GCR-2141
*AUC
#AUC
from
GC-mel
mel

Fig 16B

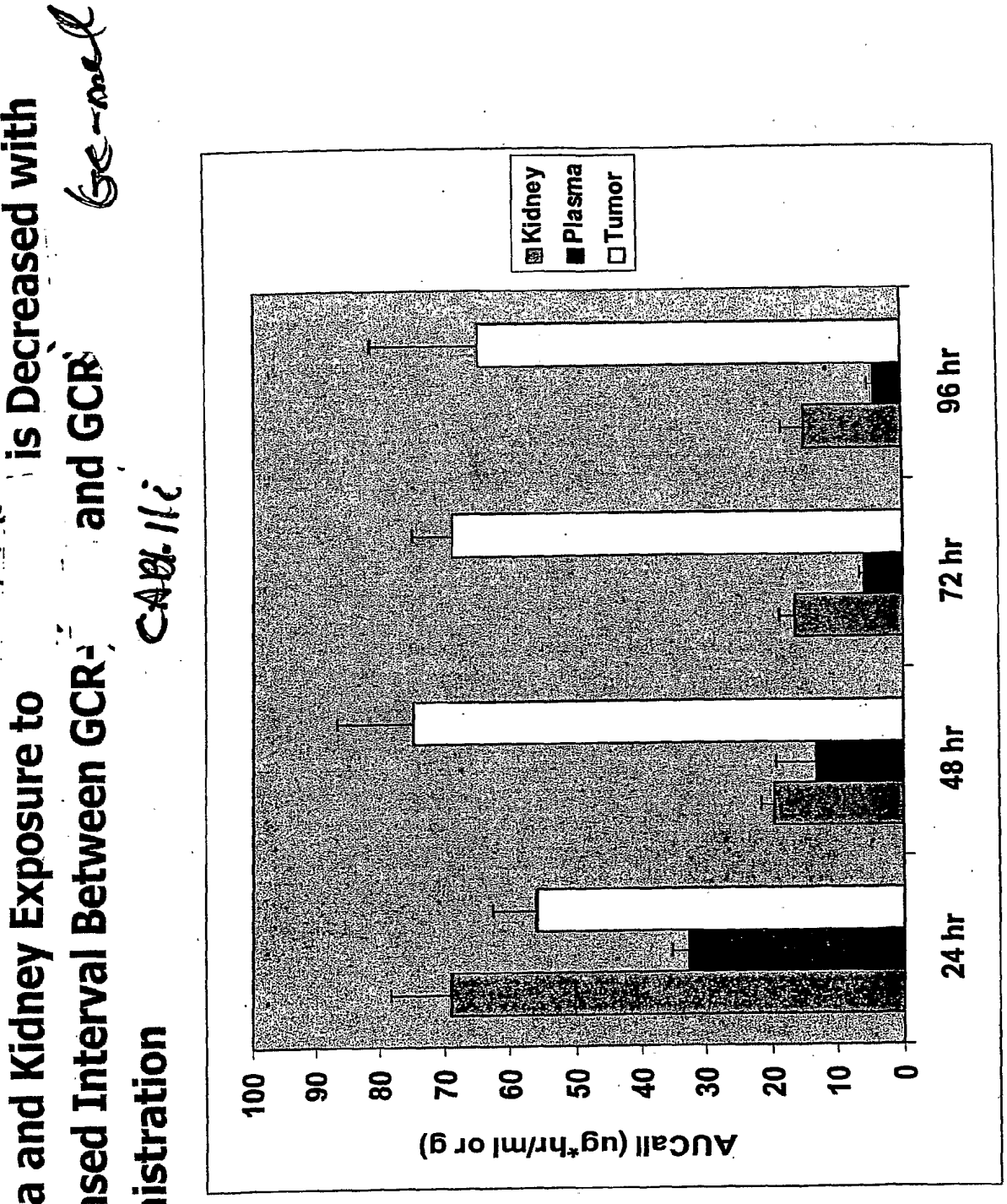
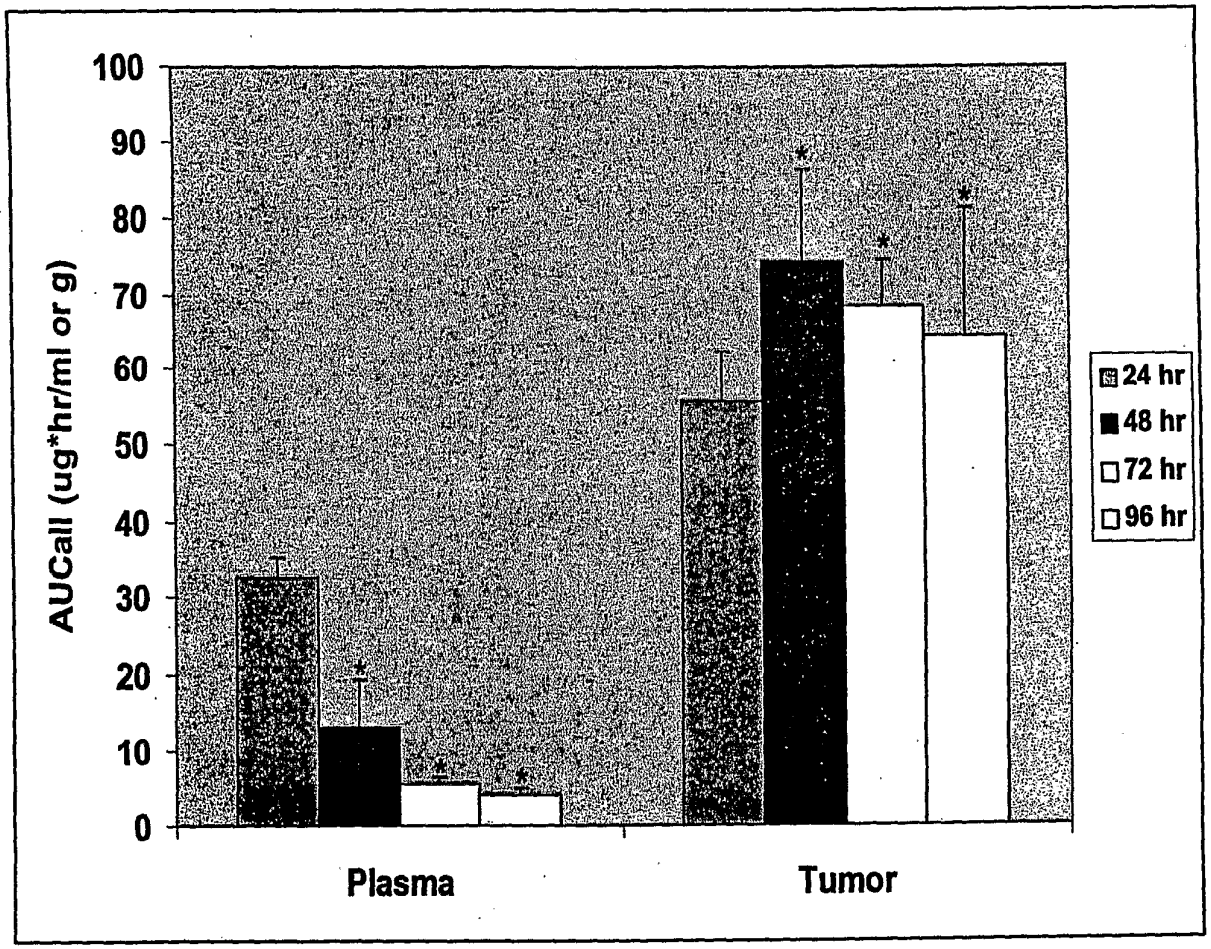

Plasma and Kidney Exposure to
Increased Interval Between GCR
Administration
is Decreased with
and GCR
Gemcitabine
CAB-IIc
Kidney
Plasma
Tumor
AUCall (ug*hr/ml or g)
100
90
80
70
60
50
40
30
20
10
0
24 hr
48 hr
72 hr
96 hr

Fig 17

Efficacious Tumor Melphalan Exposures Achieved at Each Time Interval While Systemic Melphalan Exposure Decreased

Fig 8I



*p<0.05

- Efficacy demonstrated at 24 hr interval in TLS174T xenograft mouse model

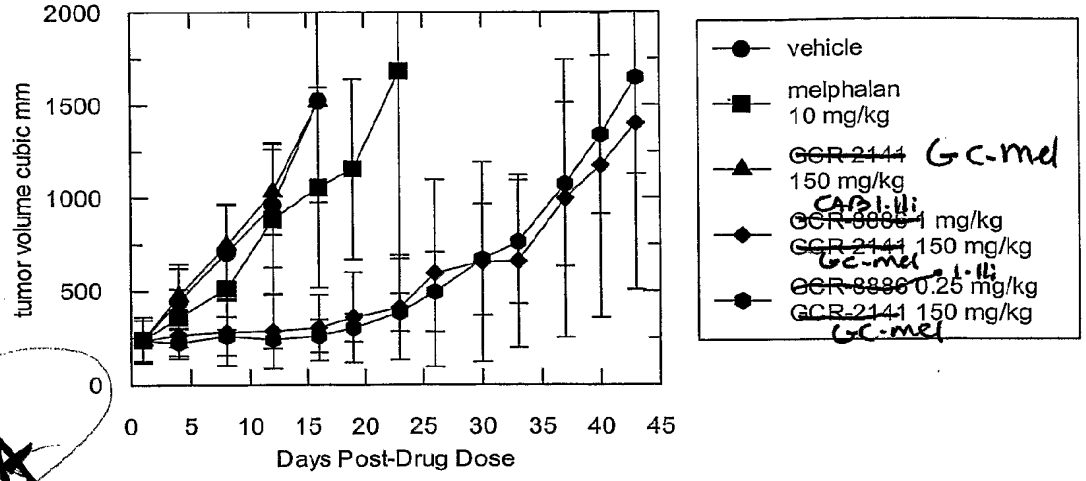
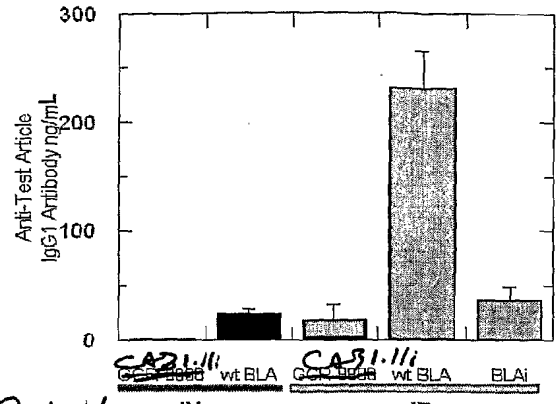

2000
1500
1000
500
0
tumor volume cubic mm
0 5 10 15 20 25 30 35 40 45
Days Post-Drug Dose
vehicle
melphalan
10 mg/kg
GCR-2144
150 mg/kg
GCR-8886 1 mg/kg
GCR-2141 150 mg/kg
GCR-8886 0.25 mg/kg
GCR-2141 150 mg/kg

FIG 9A

04-072 CA3 1.1i

~~GCR-8886~~ Poor Immunogen in Mice After Multiple IV or IP Administrations



CA3 1.1i ~~GCR-8886~~ weakly immunogenic after multiple IP doses in alum- similar to BLAi

FIG 20

04-066 completed

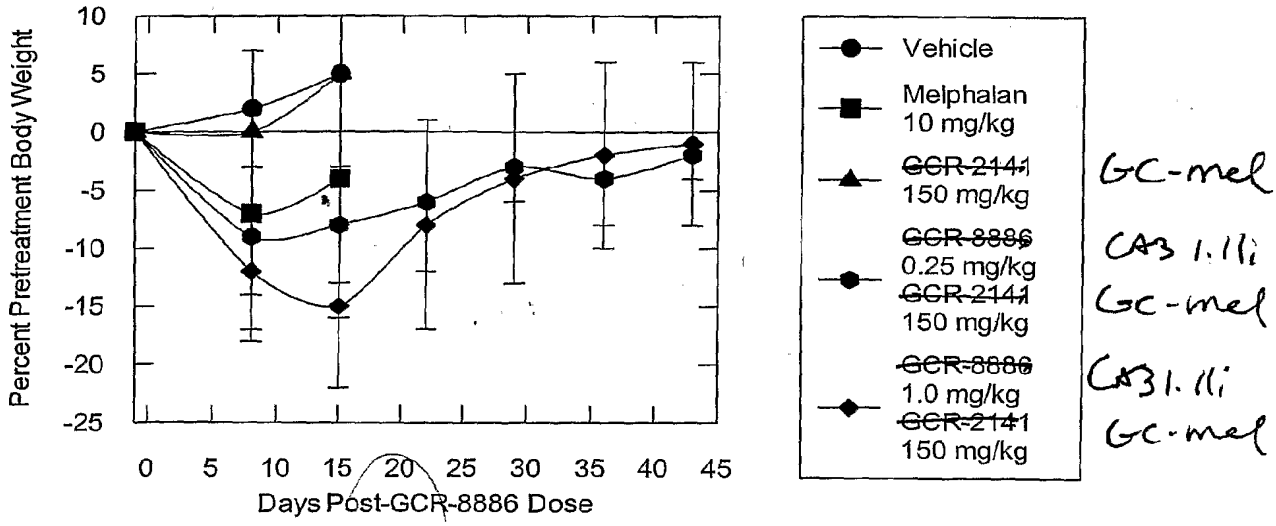


FIG 19B

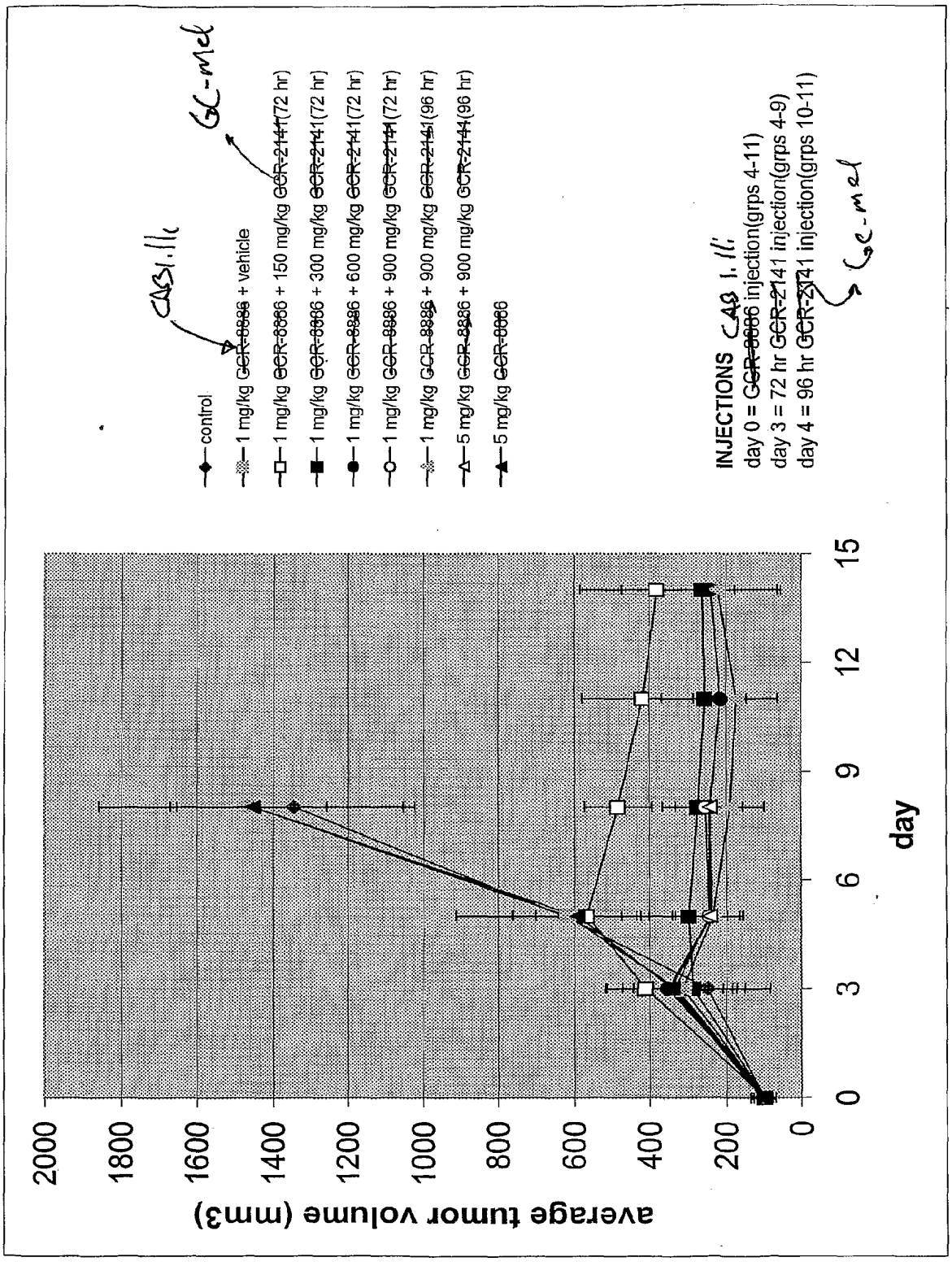

average tumor volume (mm3)
2000
1800
1600
1400
1200
1000
800
600
400
200
0
0
3
6
9
12
15
day
control
1 mg/kg GCR-8886 + vehicle
1 mg/kg GCR-8886 + 150 mg/kg GCR-2141 (72 hr)
1 mg/kg GCR-8886 + 300 mg/kg GCR-2141 (72 hr)
1 mg/kg GCR-8886 + 600 mg/kg GCR-2141 (72 hr)
1 mg/kg GCR-8886 + 900 mg/kg GCR-2141 (72 hr)
1 mg/kg GCR-8886 + 900 mg/kg GCR-2141 (96 hr)
5 mg/kg GCR-8886 + 900 mg/kg GCR-2141 (96 hr)
5 mg/kg GCR-8886
INJECTIONS
day 0 = GCR-8886 injection(grps 4-11)
day 3 = 72 hr GCR-2141 injection(grps 4-9)
day 4 = 96 hr GCR-2141 injection(grps 10-11)

Figure 21

~~04-105~~ – Avg. % Body Wt loss – ~~GCR-2141~~ injection 72 hrs (Study Day 9) post GCR-8886 injection

GC-mel

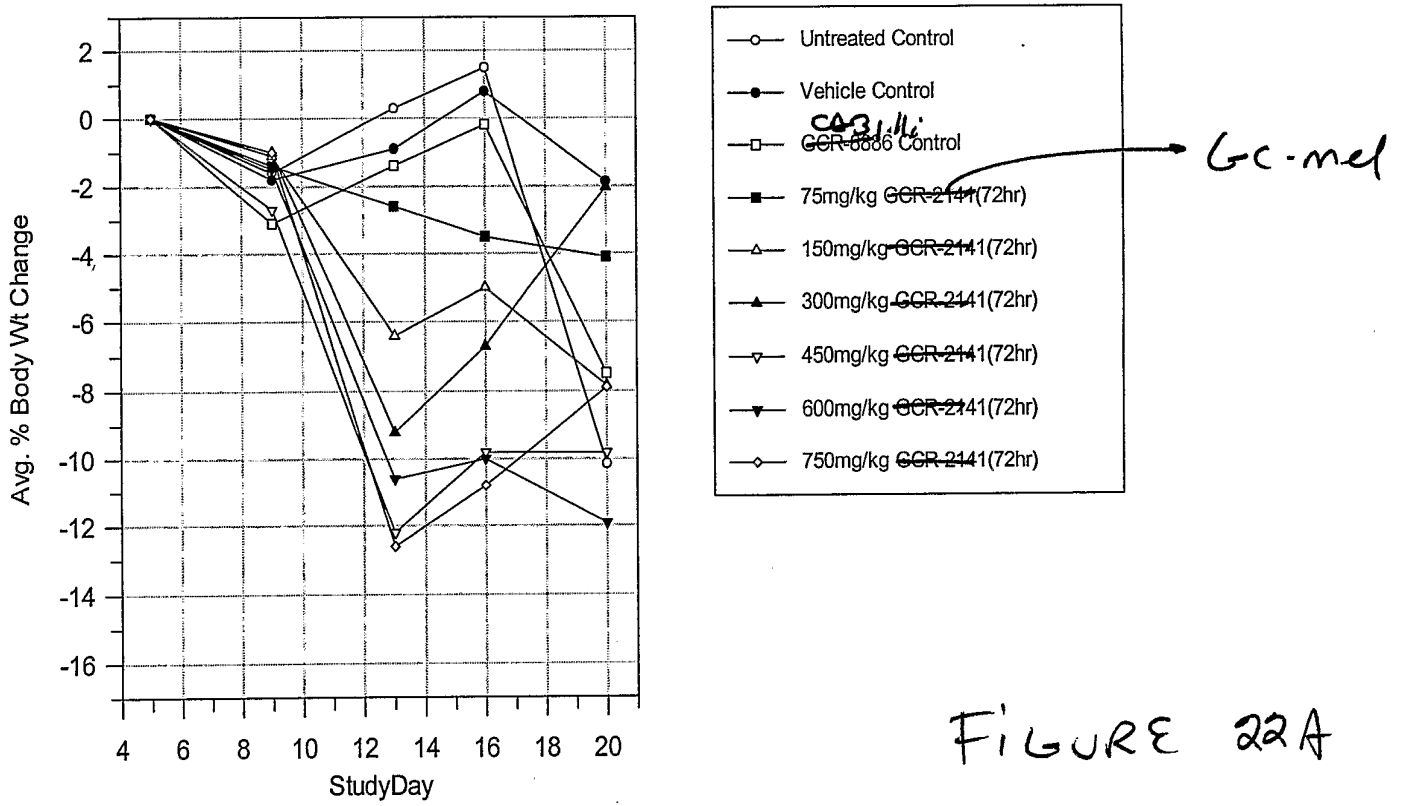


FIGURE 22A

~~04-105~~ – Avg. % Body Wt loss – ~~GCR-2141~~ GC-mel injection 96 hrs (Study Day 10) post ~~GCR-8886~~ CAB 1;11 injection

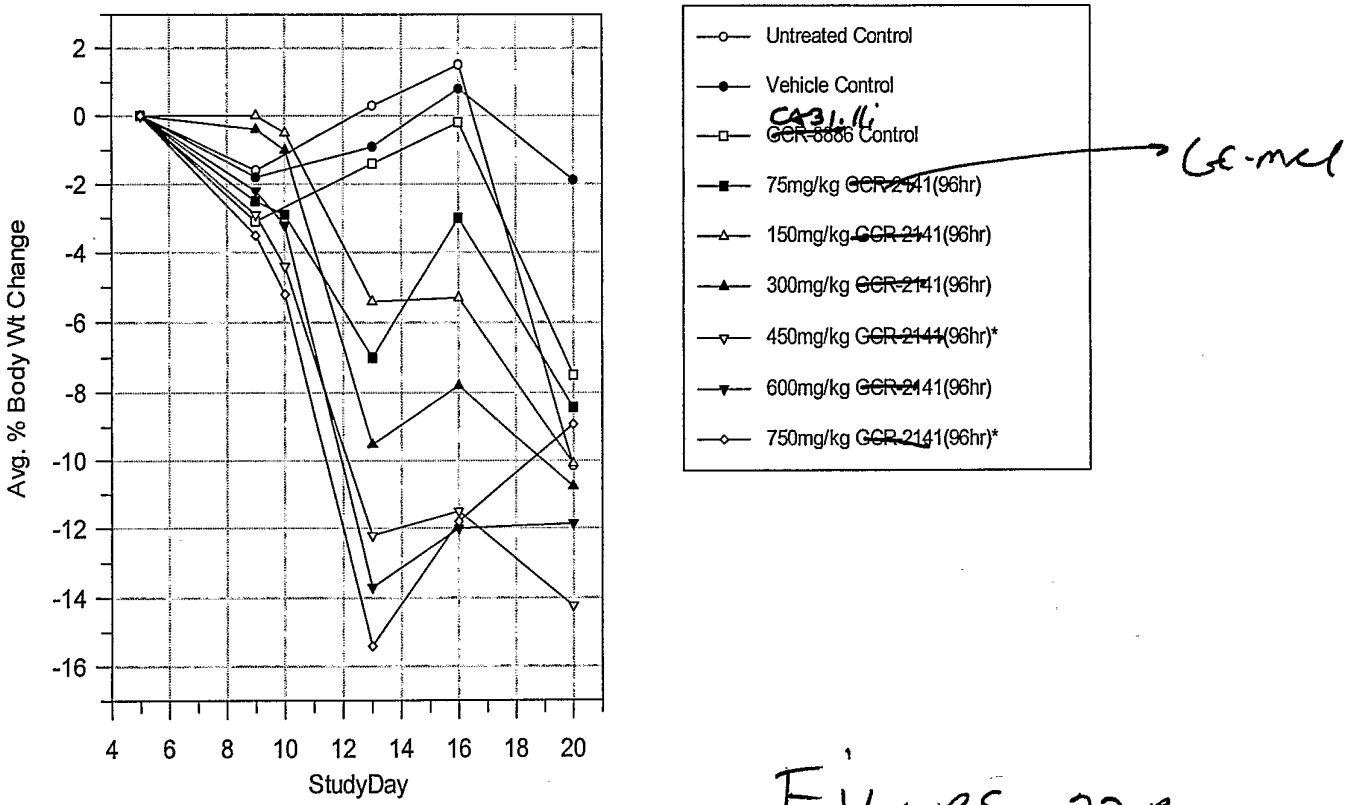


FIGURE 22B

CABILLI

Plasma ~~GCR-8886~~ concentration-time profile in rats

Results

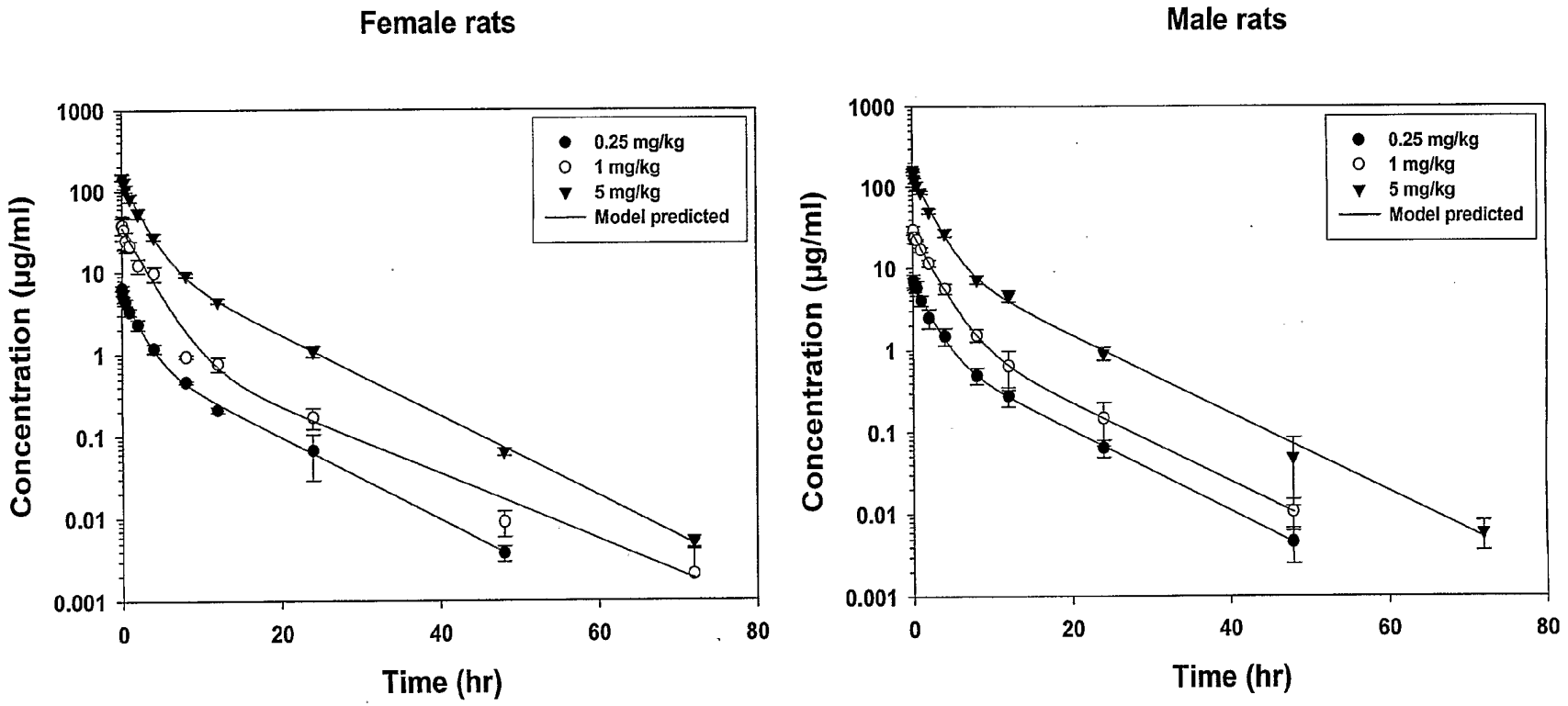


FIG 23

Plasma GCR-8886 concentration-time profiles in rats

Results

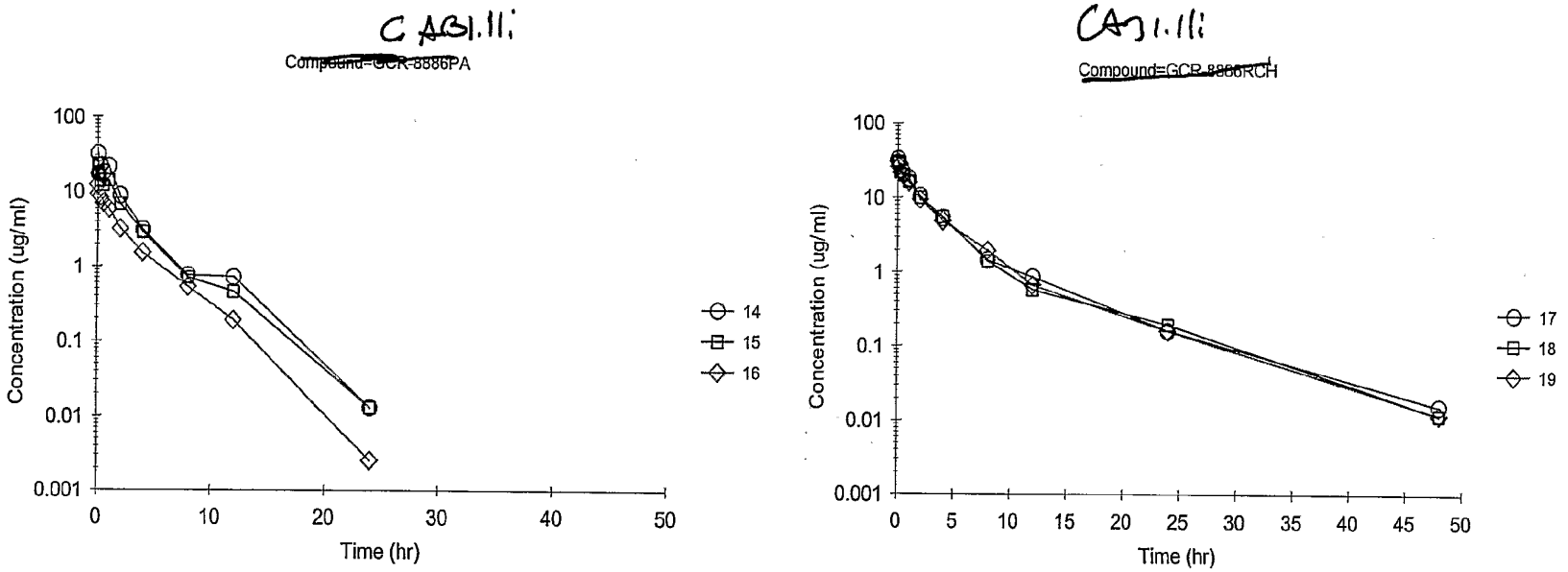
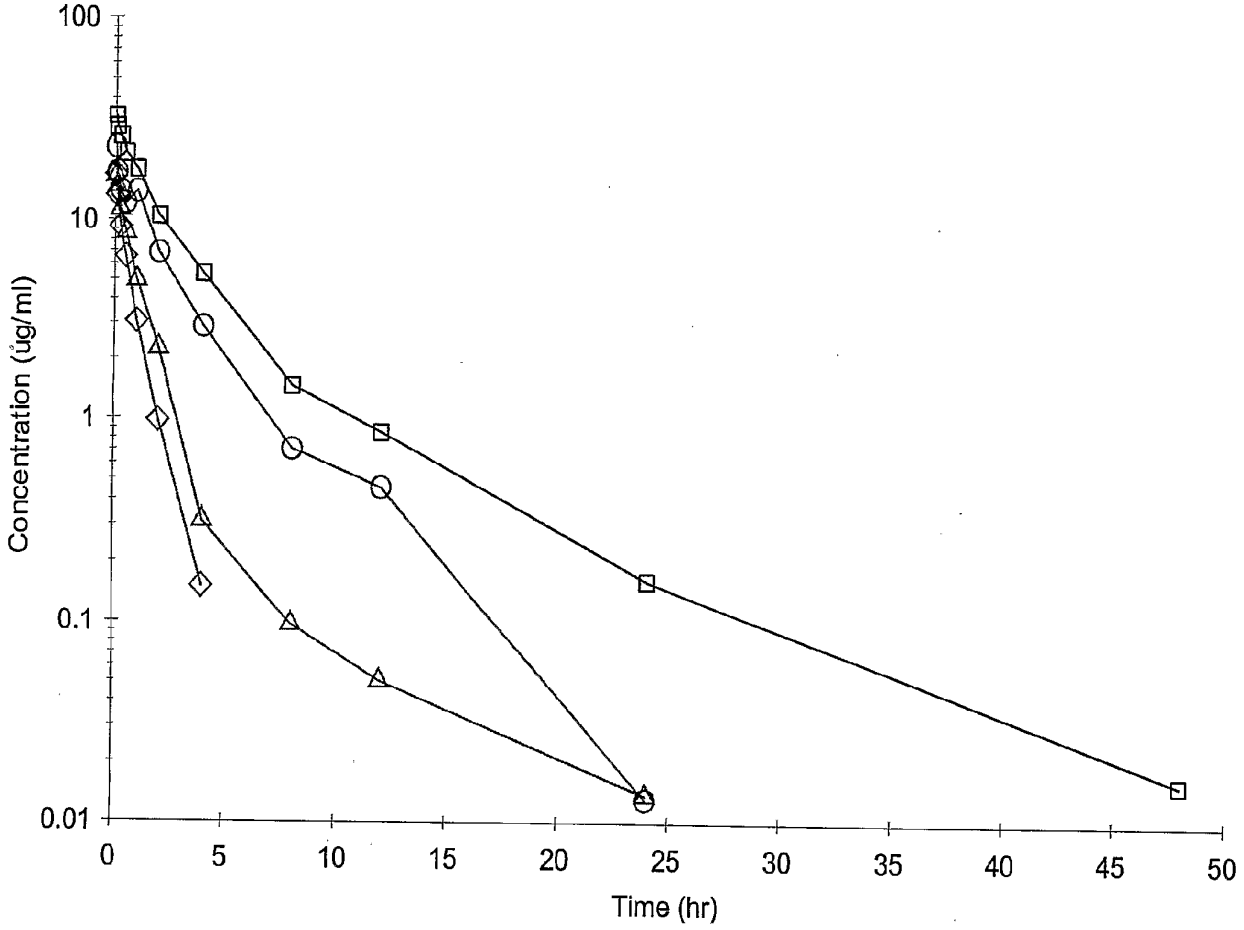


Fig 2A

Plasma concentration-time profiles in rats

Results



Each profile represents data from a single rat.

GCR-8886 concentration-time profiles following 2 weekly doses

Results

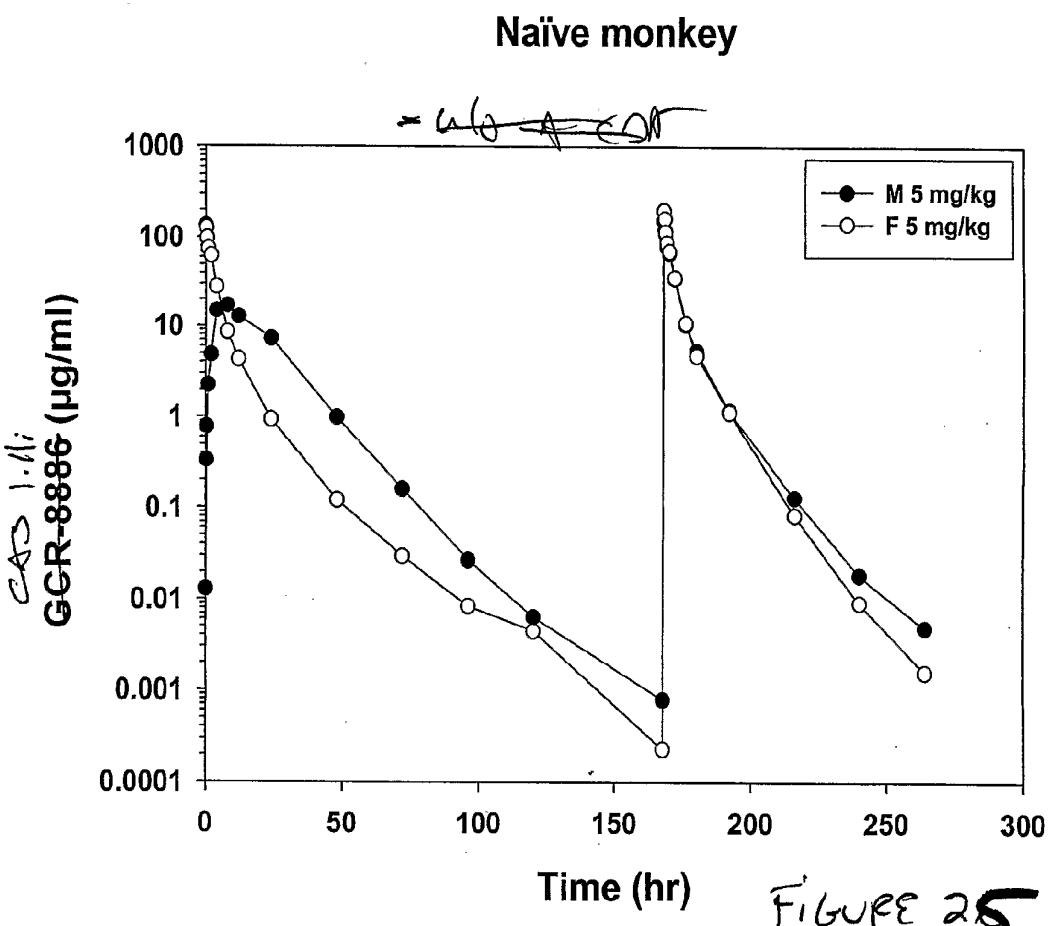


FIGURE 25

● Possible extravascular injection for the first dose

WO 2005/111078

52/53

PCT/US2005/012270

CAB 1.11i

~~GCR-8886~~ PK parameter estimates with or without CEA coadministration

Results

CAB 1.11i

~~GCR-8886~~ (1 mg/kg)

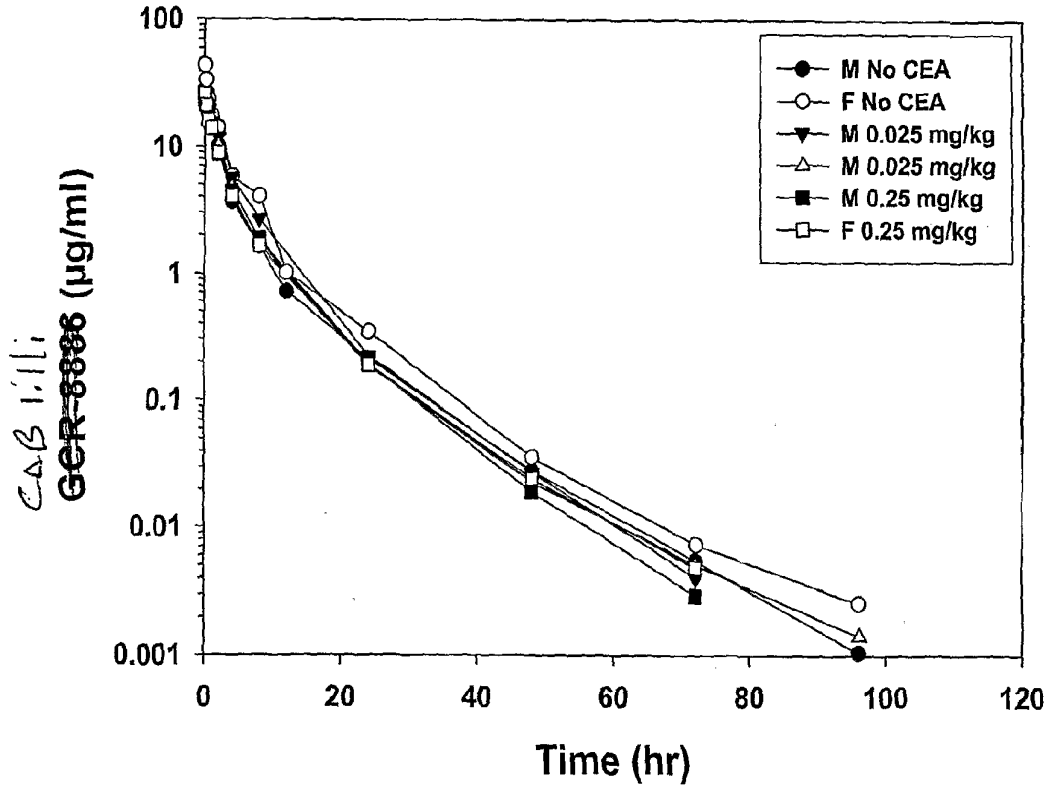


Fig 26